

**Espacenet****Bibliographic data: JP 2006296694 (A)****DECOMPOSITION METHOD OF HALOGENATED ORGANIC COMPOUND**

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Abstract of JP 2006296694 (A)

PROBLEM TO BE SOLVED: To solve problems that a conventional radiolysis method produces alkaline waste liquid after irradiation and requires a secondary treatment such as neutralization and that the absorbed dose necessary for the decomposition is very high, 1,000 kGy or more, and its treatment cost is too high for the practical application. ; SOLUTION: This decomposition method treats the halogenated organic compound by adding organic solvent and/or water to a water-free treatment object solution containing halogenated organic compound or adding organic solvent to a water-containing treatment object solution containing the halogenated organic compound and irradiating radiation to promote the decomposition of the halogenated organic compound in the solution. The organic solvent has a dielectric constant higher than that of the solvent contained in the treatment object solution. ; COPYRIGHT: (C)2007,JPO&INPIT

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(54) 【発明の名称】 ハロゲン化有機化合物の分解方法

(57) 【要約】

【課題】

従来の放射線分解方法は、照射後の廃液がアルカリ性であり、中和等の二次処理が必要であるという問題、及び分解に必要な吸収線量が1 0 0 0 k G y 以上と非常に高く、実用的には処理コストが高いという問題があった。

【解決手段】

ハロゲン化有機化合物を含む非含水被処理液では有機溶剤及び／又は水を加え、ハロゲン化有機化合物を含む含水被処理液では有機溶剤を加え放射線を照射することにより溶液中のハロゲン化有機化合物の分解を促進し、処理する。有機溶剤は、被処理液に含まれる溶媒より高い誘電率をもつものである。

【選択図】 なし

【特許請求の範囲】

【請求項1】

放射線照射により溶液に含まれるハロゲン化有機化合物を処理する方法であって、被処理溶液に有機溶剤及び／又は水を加えることを特徴とする溶液中のハロゲン化有機化合物の分解処理方法。

【請求項2】

被処理溶液に加える有機溶剤の誘電率が、被処理溶液の溶媒より高いことを特徴とする請求項1記載の方法。

【請求項3】

被処理溶液に加える有機溶剤が一種以上であることを特徴とする請求項2記載の方法。

【請求項4】

被処理溶液に含まれるハロゲン化有機化合物が、ハロゲン化ダイオキシン類、ポリハロゲン化ビフェニル類及びハロゲン化ベンゼン類の少なくとも一種であることを特徴とする請求項1乃至請求項3のいずれかに記載の方法。

【発明の詳細な説明】

【技術分野】

【0001】

本発明は、種々のハロゲン化有機化合物を含む産業廃液、ポリハロゲン化ビフェニル溶液、ハロゲン化ダイオキシン類で汚染した物質から抽出除去したことにより生じるハロゲン化ダイオキシン類を含む溶液、ダイオキシン類分析廃液、及びハロゲン化ベンゼン類の溶液の分解処理に関する。

【背景技術】

【0002】

上記、種々のハロゲン化有機化合物を含む産業廃液は、熱処理、化学的処理、光分解、

プラズマ分解等により処理されている。

ダイオキシン類分析廃液及びダイオキシン類分析済み溶液に関しては、適切な処理方法が開発されるまで手をつけずに保管している状態である。

【0003】

この問題を解決する手段として、トランスフォーマーオイル中のポリ塩化ビフェニルをガンマ線照射により分解する方法（例えば、非特許文献1）やダイオキシン類で汚染した物質から有機溶剤で抽出したダイオキシン類を含む溶液に放射線照射することにより、ダイオキシンを分解する方法（例えば、特許文献1）が例示される。

【非特許文献1】ブルース・ジェイ・ミンチャー(Bruce J. Mincher)、外4名、「トランスフォーマーオイル中のポリ塩化ビフェニルの放射線分解速度の向上 (Increasing PCB radiolysis rates in transformer oil)」、ラディエーション・フィジックス・アンド・ケミストリー (Radiation Physics and Chemistry)、(オランダ)、エルゼビア (Elsevier)、2002年、第65巻、p. 461-465

【特許文献1】特開2000-334205号公報

【発明の開示】

【発明が解決しようとする課題】

【0004】

非特許文献1記載の処理方法は、トランスフォーマーオイル中のポリ塩化ビフェニルの放射線分解に関するものであり、アルカリ性イソプロパノールを添加することにより、イソプロパノールから生成したアセトンアニオンからの電子移動を含む連鎖反応機構で分解速度を向上させるものである。しかし照射後の廃液がアルカリ性であり、中和等の二次処理が必要であるという問題があった。

特許文献1の処理方法は、ダイオキシン類で汚染された物質又は液体を、有機溶媒で抽出処理してダイオキシン類を有機溶媒へ抽出し、その抽出有機溶媒に放射線を照射することによりダイオキシン類を分解処理する方法に関する。しかし、分解に必要な吸収線量が1000kGy以上と非常に高く、実用的には処理コストが高いという問題があった。

【課題を解決するための手段】

【0005】

本発明では、上記の問題を解決するために、ハロゲン化有機化合物を含む非含水被処理液では有機溶剤及び／又は水を加え、ハロゲン化有機化合物を含む含水被処理液では有機溶剤を加え放射線を照射することにより溶液中のハロゲン化有機化合物の分解を促進し、処理する。添加する有機溶剤及び／又は水は、被処理液に含まれる溶媒より高い誘電率、すなわちおよそ20以上の誘電率をもつものであり、高い誘電率を持つ溶剤を添加して放射線を照射することにより、多量に生成する溶媒和電子がハロゲン化有機化合物の脱塩素化反応（低塩素化反応）を促進し、分解に必要な吸収線量を著しく低減する。

有効な高誘電率溶剤としては、脂肪族アルコール類、ジオール類、アセトアミド類、水及びこれらの混合液が例示される。添加する有機溶剤、水の量は限定しないが、ハロゲン化有機化合物、あるいはハロゲン化有機化合物を含む溶液中の溶媒と相分離を起こさない範囲とすることが好ましい。

【0006】

本発明はハロゲン化有機化合物を含む溶液に、誘電率の高い溶剤を添加した後、放射線を照射することにより発生した添加物由来の活性種で溶液中のハロゲン化有機化合物を分解することを特徴とするものであり、放射線の種類、線量率及び線量を限定するものではない。

【発明の効果】

【0007】

以上述べてきたように本発明によれば、ハロゲン化有機化合物を含む溶液に、アルコール等の誘電率の高い溶剤を添加することにより、ハロゲン化有機化合物からの放射線照射による脱塩素反応が促進され、ハロゲン化有機化合物が低線量で容易に分解され、通常の廃液として処分できる程度にまでハロゲン化有機化合物の濃度を低減できる。また、ハロ

ゲン化有機化合物を含む溶液に誘電率の高い溶剤を添加し照射するのみで、中和等の二次処理を必要としない。

本発明は、種々のハロゲン化有機化合物を含む産業廃液、ポリハロゲン化ビフェニル溶液、ハロゲン化ダイオキシン類溶液、ハロゲン化ベンゼン類の溶液に含まれるハロゲン化有機化合物を、容易、かつ効率的に分解することを課題として研究の結果完成されたものである。

【発明を実施するための最良の形態】

【0008】

本発明者は、溶液中のハロゲン化有機化合物を放射線照射により分解するに際し、被処理液に各種の有機溶剤及び／又は水を添加して実施することにより、分解率が著しく向上することを見出し、本発明を完成するに至った。これは添加する各種有機溶剤及び水が、ハロゲン化有機化合物からの脱塩素化反応（低塩素化反応）及び分解を促進するために分解率が上がると考えられる。

【0009】

上記添加する有機溶剤としては、たとえばメタノール、エタノール、プロパノール、エチレングリコール、プロパンジオール等があげられる。これらは単独、及び混合液として使用されることができる。また、水との併用も可能である。被処理溶液に含まれる溶媒に対する添加する有機溶剤及び／又は水の添加比率は、ハロゲン化有機化合物溶液と相分離を起こさない程度が好ましい。

【実施例】

【0010】

以下、本発明を実施例に基づいて説明する。

（実施例1）

ハロゲン化有機化合物の一つであるペンタクロロベンゼンを、ノナンとエタノールの混合液、又はノナンとエタノールとエチレングリコールの混合液に溶解させ、 ^{60}Co ガンマ線を0.5～15kGy照射した後に、ペンタクロロベンゼンの濃度を液体クロマトグラフで分析し、比較した。その結果を図1に示す。

即ち、図1は、ハロゲン化有機化合物の一つであるペンタクロロベンゼンを含むノナン溶液に、溶液中の溶媒の誘電率より高い誘電率をもつ有機溶剤、すなわち、エタノール、又はエタノールとエチレングリコールを添加して、ガンマ線を0.5～15kGy照射した後にペンタクロロベンゼンの濃度を測定した結果を示す図である。●はノナンとエタノールの容積比1：1の混合液中で照射した時のペンタクロロベンゼンの濃度、○はノナン、エタノール、エチレングリコールの容積比1：1：1の混合液中で照射した時のペンタクロロベンゼンの濃度を示す。

【0011】

（比較例1）

実施例1に用いたペンタクロロベンゼンをノナンに溶解させ、実施例1と同じ条件でガンマ線を照射し、ペンタクロロベンゼンの濃度を測定した。その結果を図2に示す。

即ち、図2は、ペンタクロロベンゼンを含むノナン溶液に、ガンマ線を0.5～15kGy照射した後にペンタクロロベンゼンの濃度を測定した結果を示す図である。

【0012】

（実施例2）

ハロゲン化有機化合物の一つであり、毒性等価係数をもつ全てのジベンゾーパラジオキシン及びジベンゾージベンゾフランを含むダイオキシン類をノナンとエタノールの混合溶媒に溶解させ、 ^{60}Co ガンマ線を10～320kGy照射した後、濃縮し、ガスクロマトグラフ質量分析計でダイオキシン類の濃度を測定した。その結果を表1に示す。

即ち、表1は、ハロゲン化有機化合物の一つであり、毒性等価係数のあるダイオキシン類を含む溶液に、誘電率の高い有機溶剤を添加して、ガンマ線を10～320kGy照射した後にダイオキシン類の濃度を測定した結果を示す表である。

（比較例2）

実施例2に用いたダイオキシン類をノナンに溶解させ、実施例2と同じ条件でガンマ線を照射した。その結果を実施例2とともに表1に示す。

【表1】

		ダイオキシン類の濃度											
	溶媒	0 kGy		20 kGy		80 kGy		160 kGy		320 kGy			
		実測濃度 ng/L	毒性等量 ng-TEQ/L	実測濃度 ng/L	毒性等量 ng-TEQ/L	実測濃度 ng/L	毒性等量 ng-TEQ/L	実測濃度 ng/L	毒性等量 ng-TEQ/L	実測濃度 ng/L	毒性等量 ng-TEQ/L		
実施例 2	ノナン + エタ ノール	6400	760	1860	420	146	44	0	0	0	0		
比較例 2	ノナン	6400	760	4400	974	2600	475	1440	356	48	12		

本発明は、種々のハロゲン化有機化合物を含む産業廃液、ポリハロゲン化ビフェニル溶液、ハロゲン化ダイオキシン類溶液、ハロゲン化ベンゼン類の溶液に含まれるハロゲン化有機化合物を、容易、かつ効率的に分解することを課題として研究の結果完成されたものである。

【産業上の利用可能性】

【0014】

本発明は、種々のハロゲン化有機化合物を含む産業廃液、ポリハロゲン化ビフェニル溶液、ハロゲン化ダイオキシン類溶液、ハロゲン化ベンゼン類の溶液に含まれるハロゲン化有機化合物を、容易、かつ効率的に分解することができる。

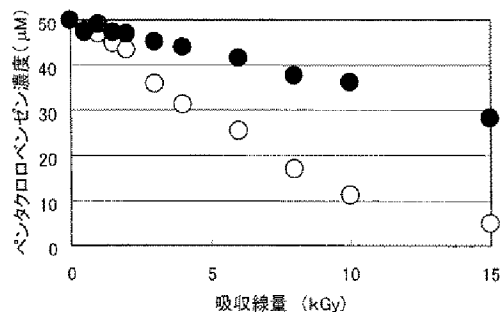
【図面の簡単な説明】

【0015】

【図1】実施例1で、ハロゲン化有機化合物の一つであるペンタクロロベンゼンを含むノナン溶液に、エタノール、又はエタノールとエチレングリコールを添加して、ガンマ線を0.5～15 kGy照射した後にペンタクロロベンゼンの濃度を測定した結果を示す図である。

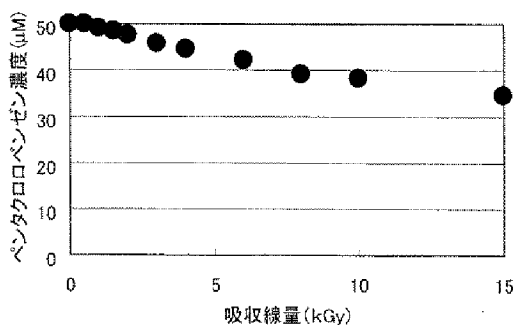
【図2】比較例1で、ペンタクロロベンゼンを含むノナン溶液に、ガンマ線を0.5～15 kGy照射した後にペンタクロロベンゼンの濃度を測定した結果を示す図である。

【図1】



● ノナンとエタノールの混合液中での放射線分解
○ ノナン、エタノール、エチレングリコールの混合液中での放射線分解

【図2】



● ノナン中での放射線分解

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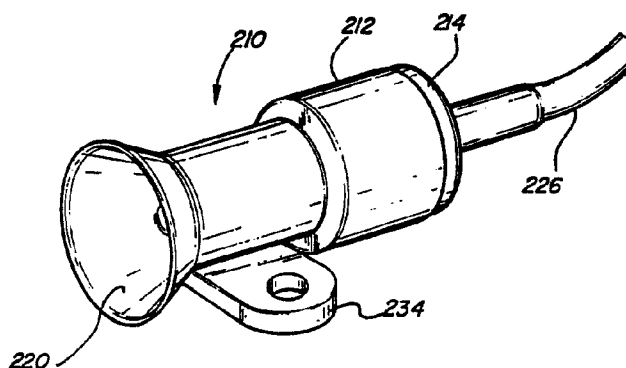
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(54) Title: IMPLANTABLE INFUSION DEVICE



(57) Abstract

An infusion port (10) for implantation adapted for providing repeated access to specific tissue within a patient and communicating with the tissue by an internal implanted catheter (52). The infusion ports according to this invention incorporate an enlarged entrance orifice (13) with a funnel shaped internal cavity which narrows down to a reduced diameter passageway (18). An articulating catheter valve (24) is provided within the passageway which normally prevents the flow of fluids through the valve but can be penetrated by an external introduced filament (32) such as a catheter. After implantation, an external filament (32) which is introduced into the port (10) is guided by the port internal cavity into registry with the catheter valve (24). Continued feeding of the filament (32) causes the catheter to pass through the valve (24). Thereafter, when a catheter (32) is inserted, therapeutic agents infused within the patient, or body fluids can be withdrawn. Alternate embodiments disclose various valve concepts (56) and means for providing a change in direction of an introduced filament inserted through the infusion device. Additional embodiments disclose the concepts of providing an antimicrobial fluid bath (98) within the device for prevention of infection and various approaches for securely connecting an internal catheter (52) to an infusion port.

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IMPLANTABLE INFUSION DEVICEFIELD OF THE INVENTION

This invention relates to a device for introducing a flexible filament into a patient such as a catheter for infusing a therapeutic agent to a desired site within the patient
5 or withdrawing a fluid, and more particularly, to such a device which is implanted such that no portion is transcutaneous. Its access portion is subcutaneous but designed so as to facilitate repeated access by the percutaneous route.

BACKGROUND AND SUMMARY OF THE INVENTION

In current human and animal medical practice, there are numerous instances
10 where therapeutic agents must be delivered to a specific organ or a tissue within the body. An example is the infusion of chemotherapy into a central vein on a recurring basis over a lengthy treatment period for widespread sites of malignant tumor. Without an infusion device for intravenous drug infusion, multiple vein punctures over a lengthy period results in progressive thrombosis, venous sclerosis, and destruction
15 of small diameter peripheral vessels. In other cases, it may be desirable to infuse chemotherapy to a localized malignant tumor site. It may be difficult or impossible to deliver an agent specifically to such a site on a regular repetitive basis without surgically implanting an infusion system. Similarly, repeated arterial access is occasionally needed for injection of an X-ray dye or contrast agent into an artery for
20 diagnostic purposes. In other situations, there is a need to remove a body fluid repetitively for analysis from a remote body site. Finally, sensing and physiological measuring devices incorporated into small diameter catheters and small diameter optical fibers are increasingly being utilized for monitoring body processes and could be more easily implemented through a properly designed access device with an
25 adequate internal diameter.

In prior medical practice, percutaneous catheters have been used to provide vascular or organ access for drug therapy or removing body fluids. Although such systems generally performed in a satisfactory manner, numerous problems were presented by such therapy approaches, including the substantial care requirements
30 by patients, e.g. dressing changes with sterile techniques, a significant rate of infection of the catheter because of its transcutaneous position, and a high rate of venous thrombosis, particularly if the catheter was located within an extremity vein.

Implantable infusion devices or "ports" have recently become available and are a significant advance over transcutaneous catheters. Presently available infusion

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ports have a number of common fundamental design features. The ports themselves comprise a housing which forms a reservoir which can be constructed from a variety of plastic or metal materials. A surface of the reservoir is enclosed by a high-density, self-sealing septum, typically made of silicone rubber. Connected to the port housing is an outflow catheter which communicates with a vein or other site within the patient where it is desired to infuse therapeutic agents. Implantation of such devices generally proceeds by making a small subcutaneous pocket in the patient under local anesthesia. The internal outflow catheter is tunnelled to the desired infusion site. When the physician desires to infuse or remove material through the port, a hypodermic needle is used which pierces the skin over the infusion port and is placed into the port.

Although presently available implantable infusion ports generally operate in a satisfactory manner, they have a number of shortcomings. Since these devices rely on a compressed rubber septum for sealing, there are limitations in the diameter of needles which can be used to penetrate the septum, since large diameter needles can seriously damage the septum. These diameter limitations severely restrict the flow rate of fluids passing through the port. In cases where it is desirable to infuse drugs using a flexible external inflow catheter, the catheter must be fed through the needle which penetrates the septum. Such catheters have an extremely small inside diameter and, therefore, impose severe limitations on fluid flow rate.

For prolonged infusion using a conventional port, the infusion needle is taped to the patients skin to hold it in position. Conventional ports do not allow the needle to penetrate deeply into the port so that a small displacement of the needle can cause it to be pulled from the port. In cases where locally toxic materials are being infused, extravasation of such materials can cause local tissue damage which can lead to a requirement for corrective surgery such as skin grafting or removal of tissue.

Presently available implantable drug infusion devices must also have a significant size to provide an acceptable target surface area for the physician who must locate the port and penetrate the septum properly with a needle. The port housing becomes bulky as the septum size increases since structure is required to maintain the septum in compression to provide self-sealing after the needle is removed. Moreover, presently available infusion ports are difficult to clear if thrombosis occurs within them or in the implanted outflow catheter, since it is difficult

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if not impossible to feed a cleaning wire through the penetrating hypodermic needle in a manner which will clear the infusion device and the internal outflow catheter. Present infusion ports have a retained volume beneath the self-sealing septum which increases the volume of drug which must be administered to enable a desired
5 quantity to reach the infusion site. This retained volume also poses problems when a physician desired to deliver drugs to the same infusion site which are incompatible when mixed. In addition, when it is desired to withdraw blood through the port, the retained volume of the prior art infusion ports comprises an area where blood clotting can occur, thus interfering with future access to the site. And finally, for present
10 infusion ports, there is a risk that the physician attempting to pierce the port septum will not properly enter it, leading to the possibility of extravasation which can cause significant undesirable consequences.

The present invention relates to a family of implantable infusion ports which provide numerous enhancements over prior art devices. In accordance with this
15 invention, an infusion port is provided which incorporates the funnel-shaped entrance orifice which narrows down to a reduced diameter guide passageway. The guide passageway terminates at an internal cavity which retains an articulating catheter valve such as a multi-element leaflet valve assembly. The port also has an exit passageway which is connected to an implanted outflow catheter.

20 Several embodiments of this invention are intended to be used by inserting a blunt instrument through the skin and into the port entrance orifice which introduces a filament such as a catheter into the port. The infusion port in accordance with other embodiments of the present invention are adapted to be used in conjunction with a sharp hypodermic access needle of conventional design which may be used
25 by itself for infusion or fluid withdrawal, or with an external inflow catheter having the needle fed through it (or vice versa) allowing a catheter to be put in position within the infusion port or fed into the implanted catheter for infusion or withdrawal of fluid. The entrance orifice has a metal surface which guides the needle to the guide passageway. The reduced diameter guide passageway of the port housing
30 can be used to accurately align the access needle and/or catheter to strike the catheter valve at a desired area so that a needle can be used to penetrate the catheter valve repeatedly without impairing the function of the valve.

According to another group of embodiments of this invention, additional features of infusion ports are described. One area of potential improvement for some

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purposes is the provision of a port designed for implantation in a patient's arm which has an access passageway for an inserted needle. The body of this port is angled upwardly slightly to facilitate access. Such an angled infusion port can also feature modifications to the entrance orifice to again further enhance the ability to access the
5 implanted port. This application further describes a valving concept for an implanted port which provides a high degree of resistance to body fluid leakage through the port and further provides a relatively low level of friction upon insertion of an external catheter, with a relatively higher degree of friction upon withdrawal of the catheter. This difference in resistance aids both in insertion of the catheter and in maintaining
10 the catheter in an inserted condition within the implanted port.

This specification also describes port design features which are best embodied in a port in which the entrance funnel is in a plane generally parallel to the mounting base of the port (i.e. the accessing needle penetrates perpendicular to the mounting base). One improvement for such ports is the provision of a physical feature such
15 as a projecting lug, flange or other protuberance which enables the clinician to determine the orientation of the implanted port through tactile examination. By knowing the port orientation, the needle and introduced filament can often be more readily inserted into the port. This series of ports also known as "chest wall" ports (named for a preferred usage) also feature a funnel-shaped entrance orifice having
20 a progressively changing included angle. The orifice starts at its outer periphery with a relatively shallow included angle which increases toward its center. This progressive change in cone angle provides two significant benefits. First, it results in a port which has a relatively shallow funnel which reduces the distance between the skin surface and the catheter valve which seals around the introduced catheter
25 or the filament and also serves to better orient and hold the introducing needle. Several of the ports according to this specification also feature means for stopping the introduced needle before reaching the catheter valve but permit the introduced catheter to pass through the catheter valve.

The infusion ports of this invention are implanted in the same general manner
30 as prior art devices. When the physician desires to infuse a therapeutic agent, remove a body fluid, or have vascular access, a filament such as a catheter is introduced into the port. The entrance orifice guides the introduced catheter or needle into a proper "docking" position with the articulating catheter valve. By pushing on the externally introduced filament, it is forced through the catheter valve,

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thereby providing an open communication pathway for the infusion of therapeutic agents, extraction of body fluids, introduction of an optical fiber, clearing by a wire, etc. The introduced filament can be fed into the outflow catheter to any extent desired. In the case of introducing a flexible catheter, a guide wire can be inserted
5 into the external catheter to increase its rigidity. The convenient access to the port and internal outflow catheter enables these elements to be cleared with a clearing wire so that they can always be cleared, avoiding the problem of permanent impaction of prior art devices. In addition, the ability to feed a guide wire into the infusion port and internal catheter of this invention enables the internal catheter to
10 be repositioned using a bent or "steerable" guide wire.

The infusion ports having an articulating catheter valve of this invention possess the advantage that they have a very small reservoir or "dead space", meaning that virtually all of the infused fluid is throughput to the desired infusion site. This invention, therefore, facilitates infusion of incompatible materials in a serial
15 fashion since very little of the previously infused fluid remains in the device when a subsequent infusion is carried out. This invention also facilitates simultaneous infusion of incompatible materials by using a multi-lumen catheter.

Another aspect of the present invention is a design for an infusion port which is configured such that a line normal to the plane formed by the entrance orifice is
20 nearly at a right angle to the exit passageway. The port access opening guides an introduced filament toward and into the outflow catheter. This approach of guiding a catheter to undergo a bend through the port can be used with conventional port designs having a self-sealing rubber septum. Other aspects of the present invention relate to providing a reservoir within an infusion port for containing an antimicrobial
25 fluid, offering enhanced protection against introduced infection. This invention is further related to various means of securely fastening an outflow catheter to an infusion port.

Additional benefits and advantages of the present invention will become apparent to those skilled in the art to which this invention relates from the
30 subsequent description of the preferred embodiments and the appended claims, taken in conjunction with the accompanying drawings.

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BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a cross-sectional view of an infusion port in accordance with a first embodiment of the present invention shown with an external catheter and obturator inserted through a leaflet type catheter valve.

5 Figure 2 is a pictorial view of a skin punch which may be used to make an incision into a patient's skin to permit insertion of an external catheter.

Figure 3 is an illustration of a stab wound formed by the skin punch shown in Figure 2.

Figure 4 is a pictorial view of the leaflet valve used with the infusion port of
10 Figure 1.

Figure 5 is a frontal view of a cup type catheter valve which is an alternate embodiment of an articulating catheter valve.

Figure 6 is a cross-sectional view of the valve of Figure 5 shown in a closed position.

15 Figure 7 is a cross-sectional view from Figure 5 showing the catheter valve in a partly open position.

Figure 8 is a sectional view taken from Figure 5 showing the catheter valve in a fully open position permitting passage of an introduced catheter.

Figure 9 is a frontal view of a catheter valve of the ball-and-seat variety which
20 is an alternate embodiment of an articulating catheter type valve.

Figure 10 is a cross-sectional view from Figure 9 showing the ball catheter valve in a fully closed condition.

Figure 11 is a cross-sectional view taken from Figure 9 showing the ball catheter valve in a fully opened condition.

25 Figure 12 is a cross-sectional of an embodiment of this invention similar to Figure 1, illustrating that an external introduced catheter may be placed well into the internal outflow catheter of the infusion port.

Figure 13 is a cross-sectional view similar to Figure 12 except showing the introduced catheter being fed through the infusion port such that its terminal end is
30 beyond the terminal end of the internal outflow catheter.

Figure 14 is a pictorial view of an infusion port in accordance with a second embodiment of this invention shown providing a change in angle for the external introduced catheter.

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Figure 15 is a cross-sectional view taken to the infusion port of Figure 14 showing the infusion port in use and showing an external introduced catheter in position for infusion of the patient.

Figure 16 is a partial cross-sectional view of an infusion port in accordance with
5 a third embodiment of this invention shown employing a pair of separated leaflet valves which provided a reservoir for an antimicrobial fluid which provides enhanced resistance against infection.

Figure 17 is a cross-sectional view of an infusion port in accordance with a fourth embodiment of this invention employing a conventional rubber septum but
10 having means for guiding a catheter or guide wire through a bend and into or beyond the port exit orifice.

Figure 18 is an infusion port in accordance with a fifth embodiment of this invention having an elliptically shaped entrance mouth.

Figure 19 is a side view of the infusion port shown in Figure 18.

15 Figure 20 is a cross-sectional view illustrating a manner of connecting an internal outflow catheter to an infusion port in accordance with this invention, incorporating an annular chamber for receiving the outflow catheter.

Figure 21 is a cross-sectional view of another means of attaching an internal outflow catheter to an infusion port according to this invention, in which the catheter
20 is placed over a smooth cylindrical surface and a compression ring is slid onto the junction.

Figure 22 is a cross-sectional view of still another approach toward connecting an internal outflow catheter to an infusion port incorporating a barbed nipple on the infusion port and a compression ring.

25 Figure 23 is another means for attaching an internal outflow catheter to an infusion port according to this invention incorporating an interlocking compression ring.

Figure 24 is a pictorial view of an infusion port in accordance with a sixth embodiment of this invention shown attached to a internal catheter.

30 Figure 25 illustrates an access needle with an external catheter being used to penetrate the infusion port shown in Figure 24.

Figure 26 is an exploded pictorial view of the infusion port of this invention illustrated in Figure 25 shown with an optional elastic ring sealing disc for use with the leaflet valve elements.

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Figure 27 is a cross-sectional view taken from Figure 24 showing the internal construction of the infusion port according to this invention.

Figure 28 is a frontal view of the elastic leaflet valve elements as shown in Figures 26 and 27.

5 Figure 29 is a pictorial view of an angled infusion port according to a seventh embodiment of this invention.

Figure 30 is a side view of the port shown in Figure 29 shown implanted within a patient and being accessed by a penetrating needle.

Figure 31 is a pictorial view of an eighth embodiment of an infusion port
10 according to this invention.

Figure 32 is a cross-sectional view taken along line 32-32 from Figure 30.

Figure 33 is an exploded pictorial view of the catheter valve of the port shown in Figures 31 and 32.

Figure 34 is an enlarged cross-sectional view similar to Figure 32 but showing
15 an accessing needle being introduced into the port.

Figure 35 is a partial cross-sectional view showing the accessing needle and catheter being more fully inserted into the port.

Figure 36 is a partial cross-sectional view showing the introduced catheter penetrating the valve assembly of the port.

20 Figure 37 is a partial pictorial view showing an introduced catheter completely passing through the articulating valve and in a proper docking position with the port for material infusion.

Figure 38 is an exploded pictorial view of another embodiment of an articulating catheter valve according to this invention.

25 Figure 39 is an exploded pictorial view of another alternate embodiment of an articulating catheter valve according to this invention.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

An infusion port in accordance with a first embodiment of this invention is shown in figure 1 and is generally designated there by reference number 10.
30 Infusion port 10 generally comprises housing 12 defining an entrance orifice 14, an inside cavity 13 which funnels down to base 20, with an exit orifice 16, and an elongated passageway 18 extending between the external orifice base, and exit orifice 16. In the embodiment shown, infusion port housing 12 is rotationally symmetrical about a central longitudinal axis passing through passageway 18. As

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is evident from Figure 1, the diameter of entrance orifice 14 is preferably several times greater than the internal diameter of passageway 18 (i.e. an area difference four times or more). The entire housing 12 can be formed in one piece from numerous polymeric materials or metals which are compatible with human or animal
5 implantation.

Positioned within passageway 18 is leaflet valve assembly 24, which is also shown in an exploded fashion in Figure 4. Leaflet valve assembly 24 is comprised of one or more thin elastic disks 26 made, for example, from silicone rubber having one or more radial slits 28 cut through them. In the embodiment shown in Figures
10 1 and 4, two disk 26 are provided, each having two slits with a right angle between them so that each defines four leaves 30. The disks 26 are oriented and stacked against one another so that slits 28 of both the disks are angularly misaligned. This misalignment is intentionally provided to enhance the sealing characteristics of valve assembly 24 when it is in its normal closed position, as shown in Figure 4.
15 Numerous other configurations for valve disk 26 can be provided, such as those incorporating any number of additional slits having various numbers of leaves.

The embodiment of infusion port 10 shown in Figure 1 includes an optional thin rubber septum 31 which acts to shield entrance orifice 14. When a foreign object is implanted in a human, the body often develops fibrous tissue around the object.
20 If an exposed concave pocket is present, such as an open entrance orifice 14, the pocket could possibly become filled with such fibrous tissue. The development of this tissue, should such occur in a patient, might restrict access into the port, and potentially could interfere with the catheter valve function. Therefore, septum 31 provided which is pre-slit at 34 to allow the introduced external filament to easily
25 penetrate the septum. Septum 31 does not, however, provide a fluid-tight barrier as in prior art infusion port which have self-sealing characteristics and is easily penetrated by a blunt instrument. The provision of septum 31 prevents tissue growth inside the housing cavity and also enables the region of housing between entrance orifice 14 and leaflet valve assembly 24 to act as a reservoir for the retention of an
30 antimicrobial fluid which aids in preventing the invasion of infectious agents during the use of infusion port 10.

In use, infusion port 10 is surgically positioned subcutaneously within the patient and mounted to suitable support tissue using conventional mounting techniques, such as sutures or surgical staples. Internal outflow catheter 52 is tunneled to the

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desired site in the body. When access is desired for the infusion of therapeutic agents, for the sampling of body fluids or for the introduction of physiological sensing elements (electrical or optical transducers, etc), a flexible external catheter 32 (or other filament) is introduced into infusion port 10, as shown in Figure 1.

5 Insertion of external catheter 32 can be facilitate using skin punch 36 as shown in Figure 2. Skin punch 36 includes a pointed flat blade 38 having a width sufficient to make a desired length of an incision 40 shown in Figure 3. Skin punch 36 includes a radially extending flange 42 which limits the depth of the incision 40. Tab 44 provides a convenient means for holding and using skin punch 36. Once external
10 catheter 32 is introduced through stab wound 40, it passes into entrance orifice 14 and is guided by the funnel shaped configuration of the housing cavity into orientation with leaflet valve assembly 24. Continued insertion of external catheter 32 causes the external catheter to penetrate leaflet valve assembly 24, causing deflection of valve leaves 30.

15 In cases where external catheters 32 are used which are quite flexible, it is necessary to provide localized stiffening of the introduced catheter to facilitate its introduction through the stab wound and into the proper docking position with leaflet valve assembly 24. For such cases, a semi-rigid guide wire or obturator 46 having a blunt end 48 can be used which is inserted through the internal passageway 50
20 of catheter 32.

Leaflet valve assembly 24 is relatively insensitive to the use of various diameters of external catheter 32, thus providing flexibility for the physician. Furthermore, the characteristics of leaflet valve assembly 24 are such that once external catheter 32 is inserted through the valve, the valve does not exert a large radially inward
25 compressive force on the catheter, thus preventing collapsing of the catheter which would seal off internal passageway 50. However, it does provide sufficient friction on the external catheter to stabilize its position.

Figure 5 illustrates a cup-type catheter valve generally designated by reference number 56. Valve 56 is another articulating type valve which can be used as a
30 replacement for leaflet valve assembly 24 shown in Figure 1. For this embodiment, a valve passageway 58 is formed which has a generally conically shaped exit nipple 60. A cup shaped closure valve 62 is provided which is supported in cantilever fashion by arm 64 which normally biases the cup closure valve into sealing engagement with exit nipple 60, as shown in Figure 6. Figure 7 illustrates catheter

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valve 56 when external catheter 32, reinforced with obturator 46 is initially penetrating valve passageway 58. During this process, external catheter 32 pushes cup closure valve 62 out of sealing engagement with valve nipple 60. Figure 8 illustrates the orientation of the elements of cup catheter valve 56 once external catheter 32 is
5 fully introduced into the infusion port.

Figure 9 illustrates another embodiment for an articulating catheter valve in the form of a ball-and-seat valve, generally designated by reference number 68. Ball-and-seat valve 68 defines a conical ball seat 70 with ball closure valve 72 which is normally biased into sealing engagement with the ball seat by arm 74. Operation of
10 ball-and-seat valve 68 is similar to the operation of cup catheter valve 56 previously described. In both cases, external catheter 32 (or another filament), which may be stiffened by an obturator 46, physically unseats the valve element to permit passage of the external catheter.

Although the leaflet, cup, and ball-in-socket catheter valves described previously
15 differ in their construction, each can be described as an "articulating" valve in that the introduced filament is accurately guided into an insertion area for the valve and deflects the valve in a predictable and repeatable manner to permit passage of a catheter or other filament. These valve types are distinguishable over prior art septums which are penetrated at random locations and do not define a predictable
20 and defined passageway for a penetrating needle which cuts through and physically damages the septum. Applicants submit that there are numerous additional articulating valve designs which achieve these desired characteristics and are fully applicable to the infusion ports of the present invention.

Figure 12 illustrates infusion port 10 described previously and shows that once
25 external catheter 32 penetrates leaflet valve assembly 24 (or any other type of articulating valve used), the external catheter can be positioned at any desired point along internal outflow catheter 52. Figure 13 is a view similar to Figure 12 but shows that external catheter 32 can be fed through infusion port 10 so that its terminal end extends beyond that of internal catheter 52. This feature allows infusion port 10 to
30 be readily adapted for angiography and angioplasty procedures.

Now with reference to Figures 14 and 15, a second embodiment of an infusion port according to this invention is shown which is generally designated by reference number 80. Infusion port 80 differs principally from infusion port 10 in that the internal cavity 81 of housing 82 is in the shape of a bent or twisted funnel or horn

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such that a line normal to the plane defined by entrance orifice 84 is generally at a right angle to the longitudinal central axis of exit passageway 86. Like the first embodiment, infusion port 80 employs an articulating catheter valve, such as a leaflet valve assembly 24 as previously described.

- 5 Infusion port cavity 81 has a smooth inside surface which is shaped to have a decreasing cross sectional area from entrance orifice 84 to exit passageway 86 for guiding external catheter 32 into registry with the exit passageway. The configuration of infusion port 80 is desirable where a large target area is needed which is generally parallel to the surface of the patients skin overlying the device. In all other respects,
- 10 infusion port 60 is constructed and used in the manner consistent with that of infusion port 10 previously described. Figure 15 provides an illustration of infusion port 80 in use for infusing a patient. Port 80 is shown fastened to support tissue 88 by sutures 90 below skin 92 of the patient.

- Figure 16 is a partial sectional view of an infusion port 94 according to a third
- 15 embodiment of this invention. This embodiment differs from those described previously in that a pair of leaflet valve assemblies 24 is provided along internal passageway 18 to define an enclosed internal cavity 98. Internal cavity 98 is provided so that an antimicrobial solution 102 can be retained as a means of inhibiting the introduction of infectious agents into the patient through the process
- 20 of infusion.

- Figure 17 illustrates an infusion port in accordance with a fourth embodiment of this invention which is designated by reference number 106. Like the second embodiment shown in Figure 14, infusion port housing 108 has an internal cavity 109 which causes an external catheter or other filament to undergo a right angle bend
- 25 as it is fed into the device. However, infusion port 106 does not incorporate an articulating catheter valve, but rather uses the conventional approach of using a compressed rubber septum 110. In use of this embodiment, a hypodermic needle 112 penetrates septum 110 and a small diameter catheter 114 is fed through needle 112. As discussed previously in connection with Figure 14, the internal surface
- 30 configuration of housing cavity 109 causes catheter 114 to be guided into and through passageway 116, and if desired, into the attached internal catheter (not shown). This embodiment also provides the advantages that a guide wire can be fed through needle 112 to clear thrombosis or other obstructions occurring within the device or in the attached internal catheter.

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Figures 18 and 19 illustrate a fifth embodiment of an infusion port 120 according to this invention which may have an articulating catheter valve as described previously, or may employ a compressed rubber septum like that of the embodiment shown in Figure 17. These figures, however, illustrate that entrance opening 122 can
5 form a generally elliptical configuration such that the target area for the infusion port has is greatest area when entering the device from a direction between alignment with the exit passageway 126, or at right angle to exit passageway. In other words, a line normal to entrance opening 122 forms an obtuse angle to the axis of exit passageway 126. Like the prior embodiments, housing 124 has a smooth internal
10 surface which is shaped to guide an introduced cavity 128 with external catheter into exit passageway 126.

Figures 20 through 23 illustrate various means for attaching an internal outflow catheter 52 to an infusion port. For the embodiment of Figure 20, the infusion port features an exit end 130 defining an annular gap 132 formed between an outer
15 tubular portion 134 of the exit outlet 134 and an inner tubular portion 136. Outflow catheter 52 is slid onto inner tube 136 and into annular gap 132. Sealing means such as a gasket or O-ring 138 can be provided to enhance the integrating of the fluid tight connection. Compression ring 140 can be used which is slid onto the connection as shown in Figure 20 to exert a compressive force on outflow catheter
20 52, further securing it to the infusion port. Compression ring 140 also acts as a stress reliever to prevent kinking of the outflow catheter 52 at its connection point to the infusion port.

Figure 21 illustrates another means for connecting outflow catheter 52 to an infusion port. In this embodiment, exit end 144 has a reduced diameter projecting
25 nipple 146 which outflow catheter 152 is slid over. Like the embodiment shown in Figure 20, compression ring 140 is provided which is slid onto the connection with Figure 20.

Figure 22 illustrates an infusion port exit end 150 which features reversibly oriented barbs 152 which serve to securely engage the inner surface of outflow
30 catheter 52. Again, compression ring 140 is used to enhance the security of the connection of the outflow catheter to exit end 150.

Figure 23 illustrates still another approach toward connecting outflow catheter 52 to an infusion port exit end 156. This embodiment, like that shown in Figure 20, defines an outer tubular portion 158, an inner tubular portion 160, with annular gap

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162 therebetween. For this embodiment, however, the inside diameter surface of outer tubular portion 158 defines groove 164. Compression ring 166 has an exterior configuration including annular barb 168 which interlocks with groove 164 when the compression ring is slid onto exit end 156.

5 An infusion port in accordance with a sixth embodiment of this invention is shown in Figure 24 and is generally designated there by reference number 210. Infusion port 210 principally comprises housing 212, outlet plug 214, and articulating valve assembly 216.

As best shown in Figures 24 and 27, housing 212 defines a funnel-shaped
10 entrance orifice 220, the function of which is to guide an access needle 218 toward its center. Although orifice 220 is shown in the shape of a circular cone, other configurations could be used such as elliptical or flattened cones could be used to define the orifice opening. Such alternative shapes could be used to decrease the profile height of the device. Any configurations used for orifice 220 must possess a
15 decreasing cross-sectional area for the purpose of guiding the access needle to a focus point. At the base of the orifice cavity shown in Figure 27 is a reduced diameter guide passageway 222. Guide passageway 222 is straight and has a diameter only slightly greater than a diameter of elements which are desired to be passed into port 210.

20 Outlet plug 214 is externally threaded which enables it to be attached to the end of housing 212 opposite entrance orifice 220. Outlet plug 214 defines an externally barbed projecting hollow post 224 which enables an internal outflow catheter 226 to be slid onto the post and attached to the infusion port as shown in Figures 24, 25 and 26. Hollow post 224 can be intentionally bent as shown in Figure 27 to prevent
25 needle 218 from passing entirely through the device in which case it could damage outflow catheter 226. As is best shown in Figure 27, once assembled together, housing 212 and outlet plug 214 define an internal cavity which accommodates leaflet valve assembly 216. As shown in Figure 27, cavity 228 defines a pair of conical surfaces, with conical surface 230 joining with guide passageway 222 and
30 conical surface 232 joining with exit plug post 224.

Mounting plate 234 is attached to housing 212 or formed by it integrally and provides a means of mounting infusion port 210 to support tissues within a patient using sutures, surgical staples, etc.

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Leaflet valve assembly 216 shown in Figure 27 includes a pair of elastic leaflet valve discs 236 and 238. Each of the elastic discs include slits extending from their geometric center and radially outward toward the perimeter of the elastic disc to define three separate flaps or leaves 240. Elastic discs 236 and 238 are stacked
5 against one another in a manner to disalign cuts 239 so that the leaves 240 of each disc overlies the cuts in the other to enhance the sealing characteristic of the leaflet valve assembly. As shown in Figure 27, when housing 212 and outlet plug 214 are assembled together, the outer periphery of elastic discs 236 and 238 are slightly compressed to provide a seal which prevents fluids from leaking around the outer
10 edges of the elastic disc elements.

Figure 26 shows an optional disc ring valve element 250 (not shown in Figure 27) which is provided to further enhance the sealing characteristics of valve assembly 216. Disc element 250 has a hole 252 through its center, which has a diameter slightly smaller than the needle or catheter which port 210 is designed to
15 accommodate. Valve element 250 is positioned to be the first element encountered by the access needle. This orientation is provided to prevent the apexes of leaves 240 from damaging valve disc 250 or interfering with its sealing capability.

Infusion port 210 in accordance with this invention is adapted to be accessed using a conventional hypodermic needle 218 with a sharp end, which can be hollow
20 or solid depending on the intended application. Needle 218 can be used by itself or with an external catheter 246, which the needle is slid through so that the needle and catheter combination can be pierced through the skin and positioned into port 210 allowing the needle to be later withdrawn, leaving catheter 246 inside port 210 to provide fluid flow into or from the patient. The introduced catheter 246 can be
25 threaded into outflow catheter 226 to any extent desired, preventing unintentional withdrawal of the introduced catheter.

Figure 25 shows infusion port 210 being accessed by a needle 18 and catheter 246 combination. When the physician desires to access port 210, needle 218 is used to pierce the patient's skin at an area adjacent the port entrance orifice 220
30 and the needle is pushed into the port. Entrance orifice 220 receives the sharp end of needle 218 and guides it toward and into guide passageway 222. The guide passageway then orients needle 218 and aims it to strike leaflet valve assembly 216 at the center of valve elements 236 and 238, which is the point of intersection of the cuts 239 defining leaves or flaps 240. Guide passageway 222, therefore, guides

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needle 218 to strike leaflet valve assembly 216 in an area where cutting or damage to the elastic disc elements is minimized since the discs are most easily penetrated at their central region where their flexibility is greatest. Elastic discs 236 and 238 are intentionally provided with three or more leaves or flaps since it is believed that a
5 leaflet valve having a single slit defining only two leaves may not provide an acceptable resistance to damage by the penetrating needle. Such susceptibility to damage could occur since such a valve configuration is not believed to provide flaps with sufficient resiliency to bend away from the introduced needle, but would instead tend to be engaged and penetrated by the inserted needle 218, leading to the
10 potential for physical damage to the disc elements.

In order to provide an acceptable resistance to damage of valve assembly 216 by needle 218, it is believed that the diameter of passageway 222 which is superimposed on disc 236 in Figure 28 and designated by reference number 254, should be no larger than one-half the diameter of the slit portion of elastic discs 236
15 and 238 which is encompassed by a circle designated as diameter 256. Passageway diameters 254 greater than that ratio would permit a penetrating needle with its sharp point to strike the leaflet valve assembly 216 at near its outer perimeter, where leaves 240 are not as supple and are more likely to be pierced by the access needle than the center portion. Controlling the position of penetration of
20 needle 218 also protects elastic disc 250 from damage which would occur if the needle struck outside of hole 252.

The conical surfaces 230 and 232 of valve cavity 228 are provided to accommodate the flexing of valve leaves 240 in both directions. When access needle 218 is inserted into infusion port 210, the leaves 240 are permitted to deflect
25 toward hollow post 224. In addition, conical cavity 232 insures that the access needle 218 or other introduced filament is properly guided to pass through hollow post 224 and into internal outflow catheter 226, if desired. Upon withdrawal of access needle 218 or catheter 246 from infusion port 210, conical surface 230 enables the leaves 240 of valve assembly 216 to be freely deflected in an opposite
30 direction.

During the step of inserting needle 218 into port 210, a positive indication of full insertion is felt by the attending physician as needle 218, which is relatively rigid, engages the bent portion of hollow post 224. This stop is provided to prevent accidental damage to outflow catheter 226. However, the introduced filament or

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catheter 246 which is more flexible than access needle 218 can be readily threaded past hollow post 224 to provide deep insertion.

In addition to permitting the insertion of a needle 218 and catheter 246 to port 210, this invention would allow a guide wire to be introduced into the port through
5 access needle 218 which could be fed through the device and into and through the internal outflow catheter 246 to remove thrombosis or other clogging problems. Various other filaments type elements could also be used with port 210 such as optical fibers, electrical conductors, remote sensing systems, etc.

Numerous materials may be used to form housing 212. Since housing 212 will
10 be subject to being struck by sharp needles which must be redirected into guide passageway 222, it is desirable to form the housing or at least the surface of orifice 220 of a hard metal material such as stainless steel or titanium or a hard ceramic. Soft materials such as plastics, if used to form entrance orifice 220 could be subject to being gouged by needle 218, preventing proper guiding of the access needle.
15 Similarly, exit outlet plug 214 is subject to being struck by a sharp needle and should also be made of a hard metal material for the reasons mentioned in connection with housing 212. Elastic discs 236, 238 and 250 can be made of numerous elastic materials such as silicone rubber.

An infusion port in accordance with a seventh embodiment of this invention is
20 shown in Figures 29 and 30 and is generally designated there by reference number 310. Port 310 is designed to be accessed using a sharp needle which passes into the port through funnel shaped entrance orifice 312. Port 310 also includes a mounting pad 314 defining a generally planer mounting surface and having apertures 316 for sutures or staples to enable the device to be secured to appropriate support
25 tissue within the patient. Internal catheters 318 is shown attached to port 310 and is tunneled to a desired site within the patient.

The embodiment shown in Figures 29 and 30 of this invention is presented to disclose two specific improvements to devices described previously, namely a modified entrance orifice 312 and an inclination of the device with respect to
30 mounting pad 314. As best shown in Figure 30, infusion port 310 is oriented such that the accessing needle 320 shown in phantom lines enters the device at an angle, designated as angle A from a plane parallel to mounting pad 314. The inclined orientation of port 310 facilitates insertion of needle 320 through the patients skin 322, as shown in Figure 30.

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The further improvement shown in Figures 29 and 30 for infusion port 310 involves a removal of the upper surface of the housing in the area defining entrance orifice 312 shown as a scalloped region 324. Removing material in that area has the effect of slightly enlarging the target area of entrance orifice 312, and also to provide
5 a smoother surface which is covered by the patients skin, thus making the device somewhat less conspicuous to the patient and possibly less irritating.

Although the features of infusion port 310 discussed in conjunction with Figures 29 and 30 are employed in a port of the type shown in Figure 1, these improvements could also be incorporated into ports having various constructions and internal
10 features including other ports which are described in this application and disclosed in the related applications.

Figure 31 illustrates infusion port 330 in accordance with an eighth embodiment of this invention. Infusion port 330 is primarily intended to be implanted in the chest wall region of a patient and generally comprises a funnel shaped entrance orifice
15 332, mounting platform 334, outlet tube 336, and a valving system which will be described in the following description.

Mounting platform 334 features apertures 338 for enabling port 330 to be secured to underline tissue within a patient using sutures, staples, etc.

As best shown in Figure 31, infusion port housing 352 also features a radially
20 projecting protuberance in the form of a lug or ledge 340 projecting away from entrance orifice 332, and overlying outlet tube 336. By providing such an irregular feature on the device housing 352, the orientation of the port, and in particular, outlet tube 336 and internal catheter 318 can be readily ascertained through palpation of the device by the clinician. As will be better described in the following paragraphs,
25 for some embodiments it is necessary to cause the introduced filament to undergo a rather sharp turn upon entrance into the device, and, therefore, knowing the orientation of the port can aid in feeding in the introduced filament. Lug 340 also provides the additional benefit of shielding implanted catheter 318 from needle sticks by the accessing hypodermic needle 320, if improperly aimed.

30 Now with the reference to Figures 32 and 34, the configuration of entrance orifice 332 can be described in more detail. As is apparent from the figures, entrance orifice 332 is in the form of a pair of joined conical surfaces having differing cone angles. The first conical surface 344 which forms the outer perimeter of the orifice defines a relatively shallow cone having a relatively large included cone angle

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identified as angle B in Figure 34. Conical surface 344 joins with a smaller diameter conical surface 346 having an included angle identified as angle C in the Figure which is smaller than angle B. The shallower conical surface 344 is provided as a means of guiding inserted needle 320 toward the apex or focus area 347 of orifice 5 312. The relatively large angle B of conical surface 344 is provided so that the distance through infusion port 330 between its top planer surface and the internal valve system is kept as small as reasonably possible while providing a large target area for needle 320. This total distance is significant in that presently employed catheters which are fed over needles have a relatively short length, i.e. approximately 10 two inches. It is desirable to allow such existing needles and catheters to be used with port 330, and at the same time, insure that the introduced catheter is securely inserted into the infusion port and engaged with the internal valve. Conical surface 346 is provided with a smaller included angle as a means of securely engaging introduced needle 330 and restraining it from radial motion once it is inserted and 15 becomes rested in focus area 347.

While the benefits of the configuration of entrance orifice 312 are achieved in accordance with the illustrated embodiment using two joined conical segments, it is fully within the scope of this invention to provide an entrance orifice defined by various other surfaces having a progressively decreasing cone angle as measured 20 as shown in Figure 34 when moving from the outer perimeter of entrance orifice 332 to the focus area 347. For example, a paraboloid surface could also be provided for orifice 332. In addition, entrance orifice 332 could be defined by a surface which is asymmetrical in the sense of not being a surface of revolution about an axis through the orifice. Many surfaces can be imagined providing the benefits of the 25 invention through providing a progressively smaller cone angle or target surface as the focus area is approached.

As is shown in Figure 34 the relatively large angle of conical surface 344 serves to provide a low height between the upper surface of infusion port 330 and articulating catheter valve 350. As mentioned previously, this is advantageous since 30 standard introduced catheters have a relatively short length and it is desirable to make sure they are fully engaged with the articulating valve to preclude inadvertent withdrawal.

The focus area 347 of entrance orifice 332 joins with passageway 348 which leads to an articulating catheter valve assembly 350. For reasons which will be

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better described later in this specification, passageway 348 is intentionally oriented with respect to the central generating axis of entrance orifice 332 at a relatively great off-axis angle, shown as angle D in Figure 32 of about 60 degrees. This off-axis orientation provides a curved passageway which is intended to prevent an introduced
5 rigid needle 320 from undergoing the turn and directly engaging articulating catheter valve assembly 350. This feature accordingly distinguishes infusion port 330 from the embodiments described previously which are either designed to be used with a blunt accessing instrument, or enable the inserted needle to pass directly through the articulating valve.

10 Housing 352 is preferably made from a hard metal material which will not be gouged or engaged by the accessing needle 320. For example, titanium or another hard metal could be used to form the entrance housing 352, or could be used merely to form the surface of entrance orifice 332.

As best shown in Figures 32 and 34, infusion port housing 352 and outlet plug
15 354 define catheter valve cavity 356. As shown in the Figures, cavity 356 is bounded by a pair of conical surfaces including conical surface 358 which joins with passageway 348, and conical surface 360 formed by outlet plug 354. As shown in the Figures, the included angle defined by conical surface 358 is greater than that of conical surface 360. The conical surfaces 358 and 360 are provided to enable
20 flexing of the elements comprising articulating catheter valve 350.

Figure 33 provides an exploded view of articulating catheter valve assembly 350. The valve is comprised of a number of individual valve elements stacked together. The first valve element encountered when passing through valve 350 from entrance orifice 332, is a ring or donut valve 362, which is comprised of a ring of elastomeric
25 material with a central circular aperture 364. Infusion port 330 can be used with introduced catheters of various diameters. Ring valve 362 is not provided to seal directly against the outer periphery of all sizes of introduced catheters, but rather provides a reinforcing function for the remaining catheter valve elements and also services to orient and center the introduced catheter, as will be described in more
30 detail below. The next two valve elements are leaflet valve discs 366 and 368. Valve discs 366 and 368 each define three or more leaves 370 which form an apex at the geometric center of each valve disc. As shown in Figure 33, the leaves of each valve disc 366 and 368 are intentionally disaligned or indexed to an offset position so that the leaves are not directly overlapping. This indexing is provided to

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enhance the sealing capabilities of catheter valve 350. The next elements encountered in valve 350 are spacer ring 374 and finally another ring or donut valve 376 with central aperture 378. Aperture 378 has a diameter which is slightly smaller than any of the catheters which infusion port 330 is designed to be used with, thus
5 providing a firm perimeter seal for the introduced catheters. The elements comprising catheter valve 350 are stacked together, inserted into valve cavity 356 and retained there through the threaded engagement between housing 352 and outlet plug 354.

Since hollow post 336 of outlet plug 354 is not oriented parallel to the plane
10 defining mounting pad 314, the hollow post is bent slightly as shown in Figure 32 as a means of orientating implanted catheter 318 along the plane defining port mounting platform 334.

Figures 34 through 37 are provided to show infusion port 330 in use, and in particular, show the process of introducing an external catheter into the device.
15 Figure 34 shows infusion port 330 implanted with a patient below the surface of skin 322. In Figure 34, a hypodermic needle 320 is shown penetrating skin 322. Needle 320 is placed through catheter 382 of conventional design such as that known as an Angiocath. Needle 320 and catheter 382 are inserted through the skin and into entrance orifice 332. Conical surface 344 initially guides the needle into conical
20 surface 346, and finally into nesting engagement in focus area 347. As stated previously, orifice 312 is made from a material which will not be gouged by needle 320, but rather will guide it into focus area 347.

Figure 35 shows accessing needle 320 being fully inserted into focus area 347 and into passageway 348. Due to the inclination of passageway 348 from the
25 entrance orifice, needle 320 cannot readily pass beyond the point shown in Figure 35. Once this position is reached, the clinician has positive feedback that the elements are oriented properly since it is apparent that the needle cannot be readily inserted any further into infusion port 310.

Once the point of Figure 35 is reached, the clinician can slide catheter 382
30 along needle 320 while holding the needle in position, thus forcing the tip of catheter 382 further into infusion port 330. Figure 35 illustrates in phantom lines that external catheters 382 undergoes a bend as it is fed into engagement with valve 350. Catheter 382 does not necessarily become oriented precisely along the longitudinal axis of passageway 348 and, therefore, does not always initially engage articulating

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catheter valve assembly 350 at its center. Ring valve element 362 serves to aid in centering introduced catheter 382 to properly orient itself with respect to the remaining valve elements. As introduced catheter 382 is forced further into engagement with the catheter 350, it passes through leaflet valve discs 366 and 368.

5 As discussed in the prior related applications, the leaves 370 can be readily opened by inserting the external catheter and their triangular shape serves to aid in centering the catheter. Finally, the introduced catheter passes through second ring valve element 376 having a relatively small aperture 378. Due to the centering functions provided by ring element 362 and the leaflet element 366 and 368, the introduced

10 catheter becomes accurately aligned with and forced through aperture 378. Aperture 378 is sized to provide a perimeter seal around the introduced catheter 382. A fully inserted catheter is shown in Figure 37.

The design of articulating catheter valve 350 according to this invention provides a number of significant features. By providing spacing ring 374, deflection of leaflet

15 valve leaves 370 in the direction of the insertion of catheter 382 is freely permitted. When the introduced catheter passes through the leaflet valves, leaves 370 are permitted to deflect as shown in Figures 36 and 37 without significant restriction caused by the presence of ring valve element 376. However, upon withdrawal of introduced catheter 382, reverse deflection of valve leaves 370 causes them to be

20 reinforced by the close proximity of valve element 362, thus providing a relatively greater amount of friction during withdrawal versus insertion of catheter 382. This difference in insertion versus withdrawal friction is a desirable feature since it allows the catheter to be freely inserted into the port, yet firmly engages the inserted catheter to prevent inadvertent withdrawal of it during infusion.

25 The differing cone angles provided by catheter valve cavity conical surfaces 358 and 360 also provide several functions. The relatively large angle of conical surface 358 is provided to place the passageway 348 in close proximity to catheter valve 350. This enhances the "targeting" function to ensure that catheter 382 strikes the catheter valve 350 at or near its center where it can be easily deflected and is guided

30 into a proper engagement with ring valve element 376. This large cone angle also serves to limit the degree of deflection of ring valve element 362, thus increasing withdrawal friction. The relatively small cone angle of conical surface 360 is provided to guide the introduced catheter smoothly into hollow post 380 and provides

clearance to permit relatively unrestricted deflection of leaflet valves 366 and 368 and ring valve element 376.

Figure 38 shows in alternate embodiment of an articulating catheter valve assembly designated by reference number 386. Catheter valve assembly 386 has
5 a number of elements identical to catheter assembly 350 described previously, and the common elements are designated by common reference numbers. Catheter valve assembly 386 differs from the previous embodiment in that spacer ring 374 is replaced with another donut or ring valve element 388, having an internal circular aperture 390. The function of ring valve element 388 is to reinforce leaves 370 of
10 valve disc 368 as a means of enhancing the sealing capabilities of catheter valve assembly 386. The diameter of aperture 390 is chosen to be larger than any introduced catheter 382 with which valve assembly 386 would be used.

Figure 39 shows yet another embodiment of catheter valve assembly according to this invention designated by reference number 394. This embodiment also
15 features a number of elements common to that of catheter valve assembly 350 which are identified by like reference numbers. Catheter valve 394, however, features a flapper type valve element 396 having a central flap or leaf 398. Flapper valve 396 is provided to act as a check valve providing enhanced resistance to reverse fluid leakage since flap 398 is actuated by fluid pressure into sealing engagement with
20 valve disc 376. Flap 398 is readily deflected upon the insertion of catheter 382 or another flexible introduced filament.

While the above description constitutes the preferred embodiments of the present invention, it will be appreciated that the invention is susceptible of modification, variation and change without departing from the proper scope and fair
25 meaning of the accompanying claims.

What is Claimed is:

1. An implantable patient infusion device for permitting access to an internal catheter by a filament such as an external catheter, wire or optical fiber comprising:
a housing having a funnel shaped entrance orifice having a decreasing
30 cross sectional area which leads to a focus area, said housing further having a passageway communicating said focus area with an exit orifice, said housing causing said filament introduced into said entrance orifice to be directed to said focus area enter and enter said passageway,

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What is Claimed is:

1. An implantable patient infusion device for permitting access to an internal catheter by a filament such as an external catheter, wire or optical fiber comprising:
a housing having a funnel shaped entrance orifice having a decreasing
5 cross sectional area which leads to a focus area, said housing further having a passageway communicating said focus area with an exit orifice, said housing causing said filament introduced into said entrance orifice to be directed to said focus area enter and enter said passageway,
an articulating catheter valve positioned within said housing passageway
10 which normally remains closed to provide resistance to flow of fluids through said valve, yet opens to permit said filament to pass through said valve enabling said filament to communicate with said internal catheter, and
means for mounting said infusion device subcutaneously.
2. An implantable patient infusion device according to Claim 1 wherein said
15 catheter valve comprises a leaflet valve having a generally circular flat disk of a resilient material with at least one cut through said disk which crosses the center of said disk.
3. An implantable patient infusion device according to Claim 2 wherein said
infusion device includes at least two of said leaflet valves which are stacked together
20 and are oriented so that said cuts of a first of said valves are not aligned with said cuts of a second of said valve disks.
4. An implantable patient infusion device according to Claim 2 wherein said
disc elements each defining three or more deflectable valve leaves.
5. An implantable patient infusion device according to Claim 2 wherein said
25 passageway has a diameter not greater than one-half of the diameter of said elastic disc element portions defining said leaves.
6. An implantable patient infusion device according to Claim 2 wherein said
housing means further defines an internal cavity within which said leaflet valve is disposed.

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7. An implantable patient infusion device according to Claim 6 wherein said internal cavity provides clearance for said valve leaves to deflect toward said exit orifice.

8. An implantable patient infusion device according to Claim 6 wherein said internal cavity provides clearance for said valve leaves to deflect toward said entrance orifice.

9. An implantable patient infusion device according to Claim 6 wherein said housing means is defined by a main housing defining said entrance orifice and said guide passageway and an outlet plug connected with said main housing defining said outlet orifice, said main housing and said outlet plug cooperating to define said internal cavity.

10. An implantable patient infusion device according to Claim 2 wherein said leaflet valve further comprises a disc element having a hole for sealing against an introduced filament.

11. An implantable infusion device according to Claim 10 further comprising a second ring valve element positioned on the side of said leaflet valve confronting said exit passageway.

12. An implantable infusion port according to Claim 10 further comprising a spacer ring placed between said leaflet valve and said first ring valve.

13. An implantable infusion device according to Claim 2 comprising first and second ring valve elements positioned between said leaflet valve and said exit orifice wherein said first ring valve element supports said leaflet valve leaves and said second ring valve element defines a perimeter seal around said filament.

14. An implantable infusion device according to Claim 1 further comprising a flapper valve element.

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15. An implantable patient infusion device according to Claim 1 wherein said catheter valve comprises a cup valve having a nipple with an exit side and a valve cup for sealing engagement with said nipple, and means for resiliently urging said cup to seal against said nipple, said cup valve oriented such that said filament
5 unseats said cup from said nipple when introduced into said infusion device.

16. An implantable patient infusion device according to Claim 1 wherein said catheter valve comprises a ball-and-seat type valve wherein said ball sealingly engages with a seat formed by said infusion device and said ball is urged to unseat from said seat when said filament is introduced into said infusion device.

10 17. An implantable patient infusion device according to Claim 1 wherein said infusion device comprises at least two of said articulating catheter valves positioned within said housing and separated to define an antimicrobial fluid reservoir.

18. An implantable patient infusion device according to Claim 1 wherein said infusion device further comprises an elastic septum covering said entrance orifice and
15 having a preformed slit therethrough.

19. An implantable infusion device according to Claim 1 wherein said valve means imposes less friction upon said filament being inserted through said valve than imposed upon said filament upon withdrawal of said filament.

20. An implantable infusion device according to Claim 19 wherein said valve
20 includes at least one leaflet valve element having leaves which deflect when said filament is placed through said valve means, and means for allowing said leaves to deflect more readily in the direction of insertion of said filament as compared to removal of said filament from said device.

21. An implantable infusion device according to Claim 1 wherein said housing
25 entrance orifice is formed from a hard material wherein a needle contacting said surface is guided into said focus area.

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22. An implantable patient infusion device according to Claim 21 wherein said housing defines stop means to limit the amount of penetration of said needle in said housing after passing through said valve while allowing more flexible introduced filaments to be threaded entirely through said device.

5 23. An implantable patient infusion device according to Claim 22 wherein said stop means comprises a curved passageway which defines the limit of insertion.

24. An implantable patient infusion device according to Claim 23 where in said accessed passageway allows said filament to be pushed through said curved passageway and into an implanted internal catheter connected to said exit orifice.

10 25. An implantable infusion device according to Claim 21 further comprising stop means within said passageway between said focus area and said valve for restricting the passage of said needle while permitting said introduced filament to pass through said passageway and engage said valve.

26. An implantable infusion device according to Claim 25 wherein said stop
15 means comprises a bend in said passageway.

27. An implantable patient infusion device according to Claim 21 further comprising an external catheter having said access needle inserted into its hollow core and said infusion device allowing the combination of said needle and said external catheter to be inserted into said device and thereafter allowing said needle
20 to be removed leaving said external catheter inside said device.

28. An implantable patient infusion device according to Claim 1 wherein said entrance orifice has a maximum cross-sectional area at least four times that of the cross-sectional area of said passageway.

29. An implantable infusion device according to Claim 1 wherein said
25 entrance orifice defines a surface having a first included cone angle around its outside perimeter and defining a second included cone angle adjacent said focus area which is smaller than said first included cone angle.

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30. An implantable infusion device according to Claim 29 wherein said first and second included cone angles are formed by joined conical surfaces.

31. An implantable infusion device according to Claim 1 wherein said housing means entrance orifice has a central axis generally coaxial with the exit orifice.

5 32. An implantable patient infusion device according to Claim 1 wherein said entrance orifice defines a generally circular perimeter lying on a plane positioned such that a line normal to said plane forms a right angle to the central axis of said exit orifice with said housing passageway shaped to guide said filament inserted into said entrance orifice to bend and become inserted through said catheter valve.

10 33. An implantable infusion device according to Claim 32 wherein said housing entrance orifice has a central axis generally perpendicular to the patient's skin and further defines a projection which can be detected by external palpation after said device is implanted which indicates the orientation of said device.

34. An implantable patient infusion device according to Claim 1 wherein said
15 entrance orifice defines a plane which is oriented such that a line normal to said plane forms an obtuse angle with respect to a central longitudinal axis through said exit orifice.

35. An implantable patient infusion device for permitting access to an internal
20 catheter by a filament such as an external catheter, wire or optical fiber, comprising:
a housing defining an entrance orifice and an exit orifice with a passageway extending therebetween, said entrance orifice having a cross-sectional open area which decreases to a focus area communicating with said entrance orifice and said passageway, causing said filament introduced into said entrance orifice to
25 be directed to enter said passageway once inserted through said entrance orifice and undergo a bend as it passes through said device, and

barrier means which normally provides resistance to the flow of fluid through said infusion device but which can be penetrated by said filament to permit said filament to pass into and through said housing passageway.

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36. An implantable patient infusion device according to Claim 35 wherein said barrier means comprises an articulating valve disposed within said passageway which is opened by contact with said filament.

37. An implantable infusion device according to Claim 35 wherein said
5 housing entrance orifice is formed from a hard material wherein a needle contacting said surface is guided into said focus area.

38. An implantable patient infusion device according to Claim 37 wherein said housing defines stop means to limit the amount of penetration of said needle in said housing while allowing more flexible introduced filaments or catheters to be threaded
10 further into said device.

39. An implantable patient infusion device according to Claim 38 wherein said stop means comprises a curved passageway which defines the limit of insertion.

40. An implantable patient infusion device according to Claim 35 wherein said entrance orifice defines a generally circular perimeter lying on a plane positioned
15 such that a line normal to said plane forms a right angle to the central axis of said passageway with said housing cavity shaped to guide said filament inserted into said entrance orifice to first bend and become inserted through said barrier means.

41. An implantable infusion device according to Claim 40 wherein said housing entrance orifice has a central axis generally perpendicular to the patient's
20 skin and further defines a projection which can be detected by external palpation after said device is implanted which indicates the orientation of said device.

42. An implantable patient infusion device according to Claim 35 wherein said entrance orifice defines a plane which is oriented such that a line normal to said plane forms an obtuse angle with respect to a central longitudinal axis through said
25 exit orifice.

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43. A method for permitting repeated access to preselected tissue within a patient by a filament such as an external catheter, wire or optical fiber, comprising the steps of:

providing an implantable infusion device having an entrance orifice, a
5 funnel shaped internal cavity and an exit orifice with an articulating catheter valve positioned between said orifices which normally resists the flow of fluids through said valve,

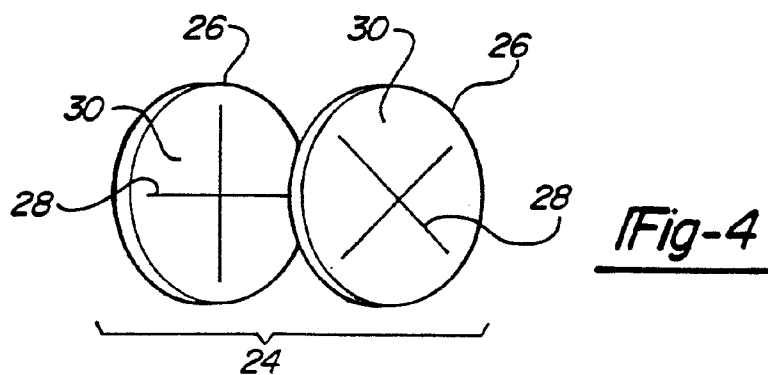
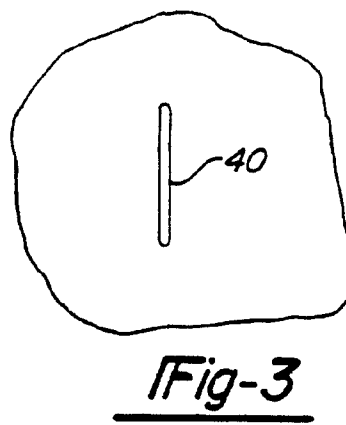
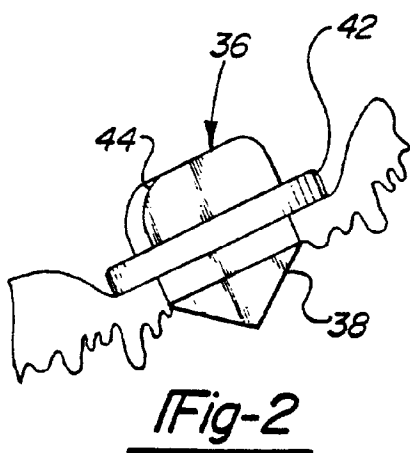
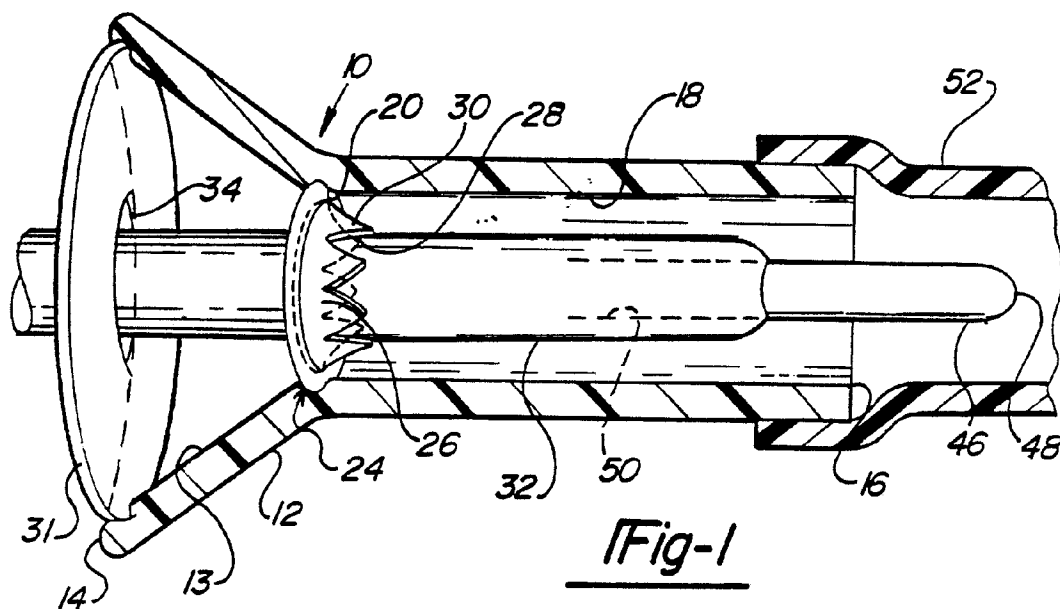
providing an internal catheter connected to said infusion device exit
orifice,

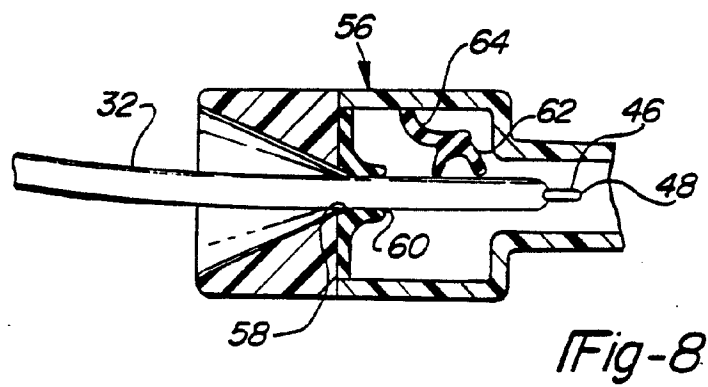
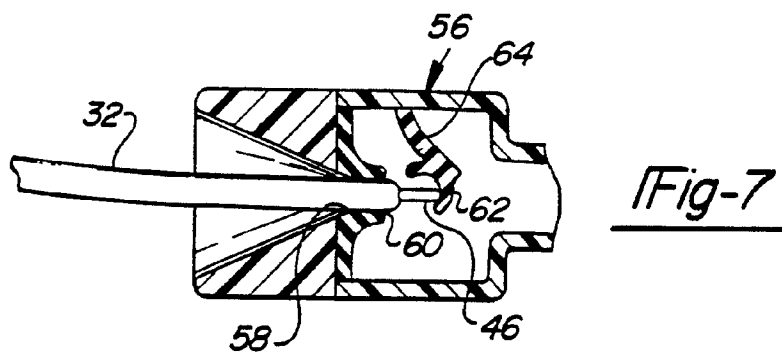
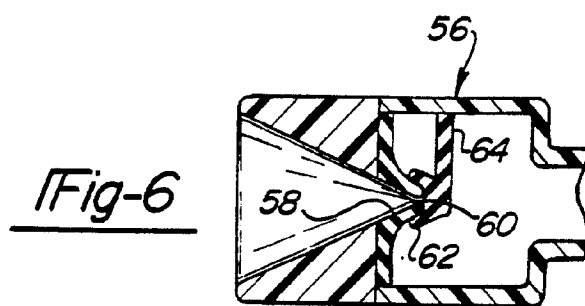
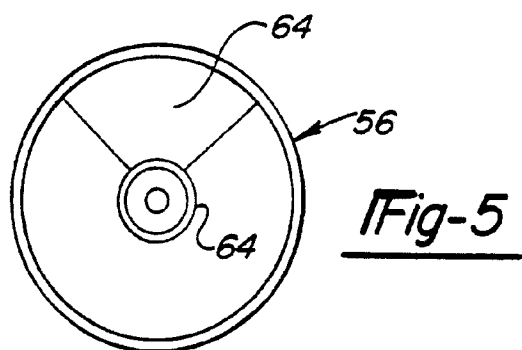
10 making an incision in the patient's skin,
implanting said infusion devices subcutaneously within a patient,
positioning said internal catheter to communicate from the infusion device to said preselected tissue,

providing a flexible filament,

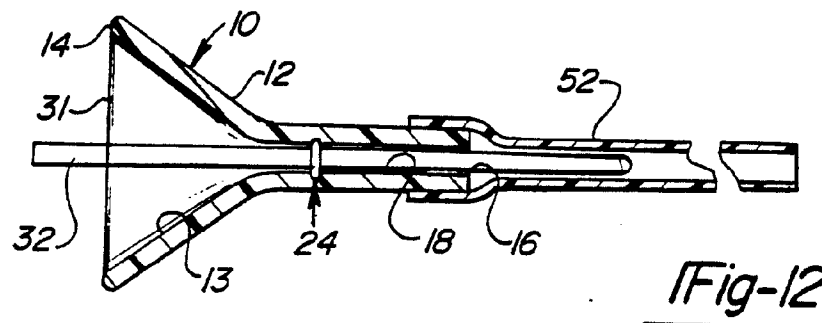
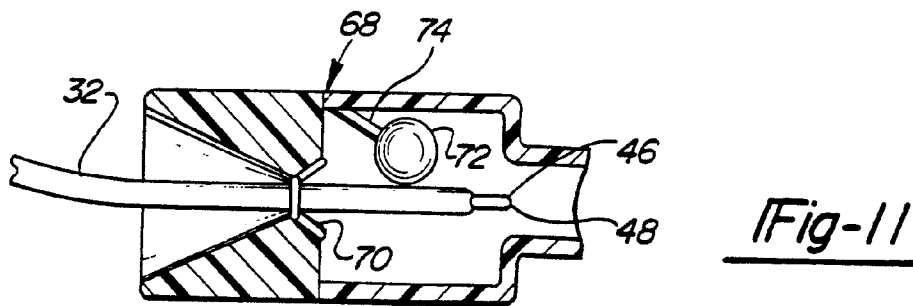
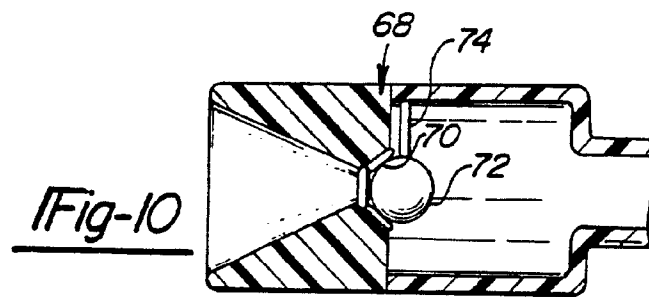
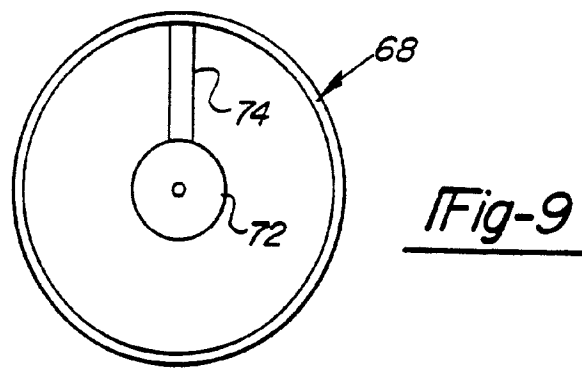
15 inserting said filament through said incision and into said infusion device receiving orifice, and

feeding said filament through said articulating catheter valve, thereby providing said access to said preselected tissue.

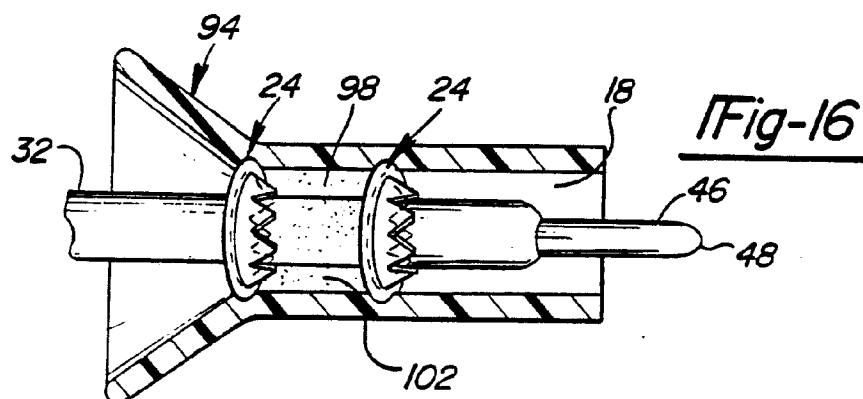
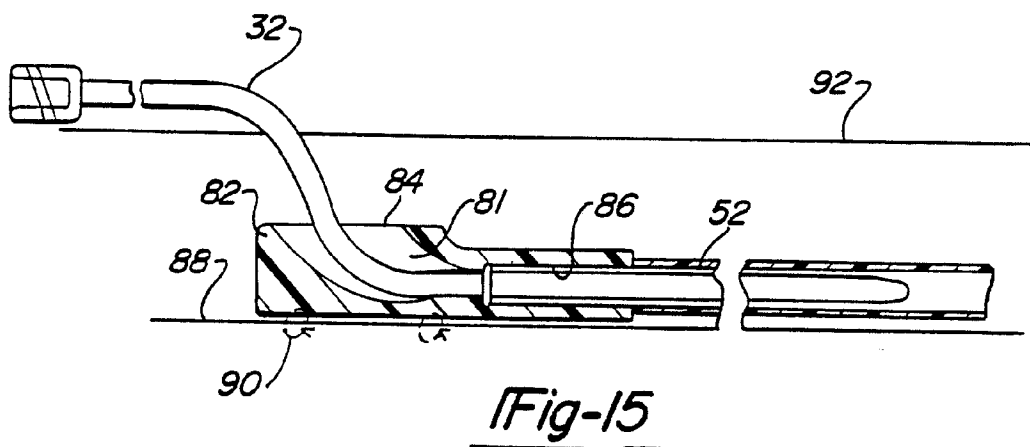
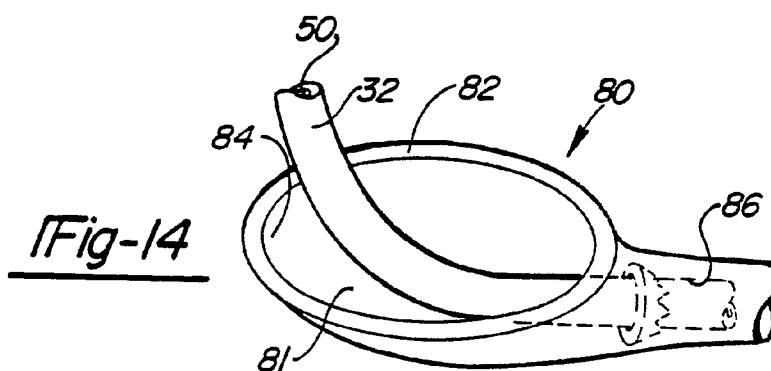
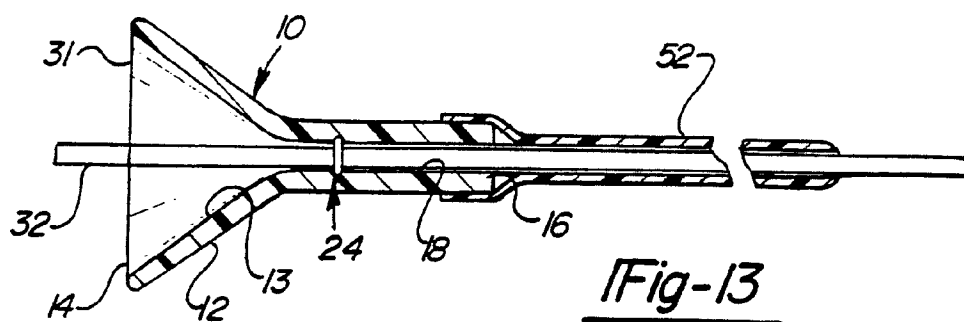




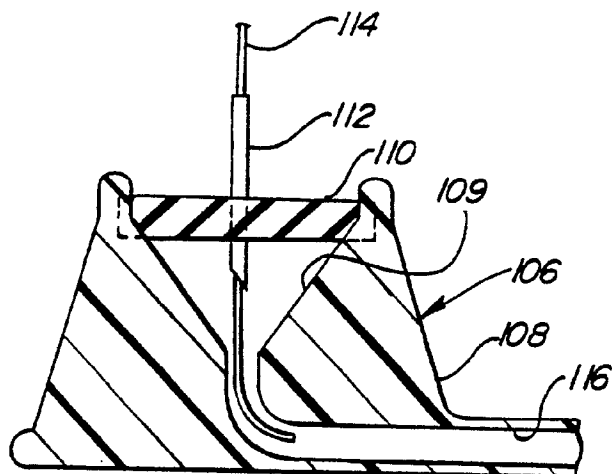
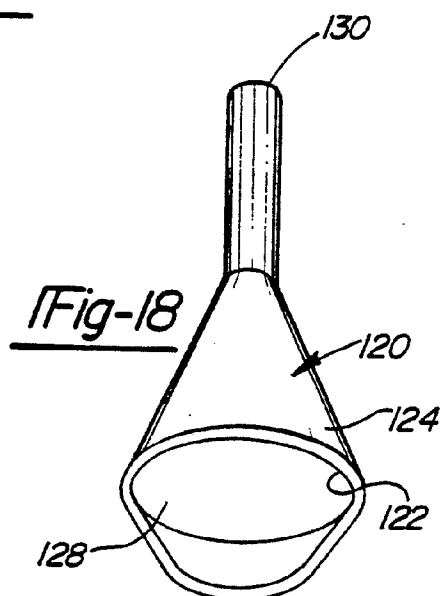
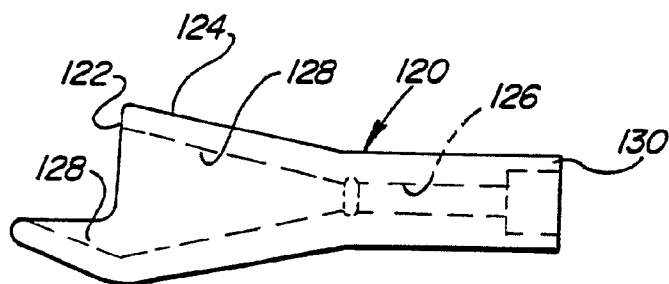
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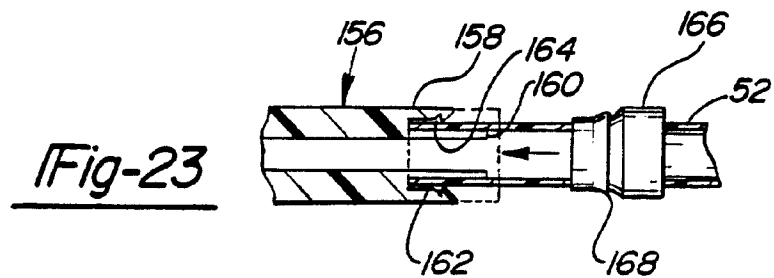
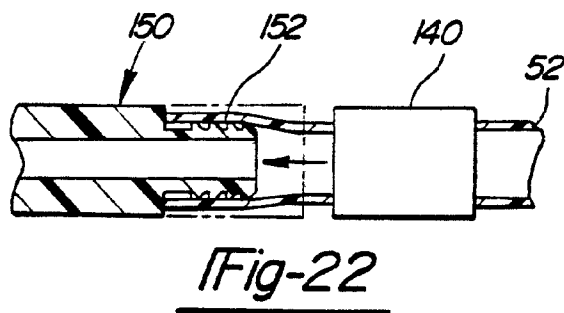
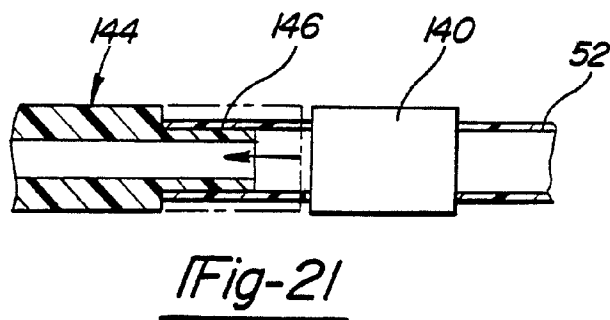
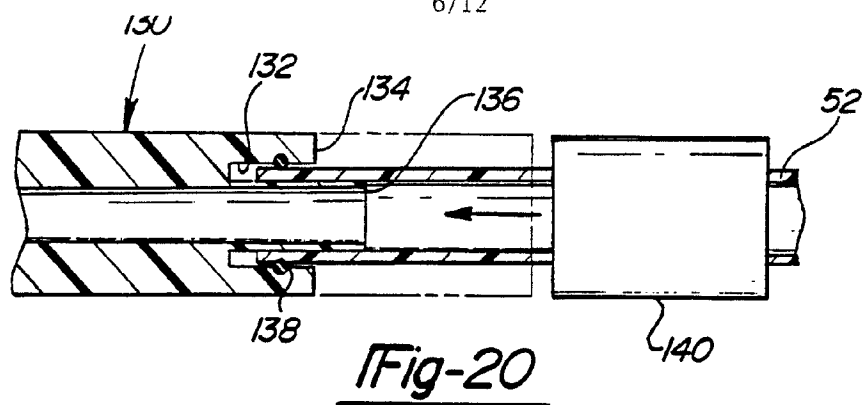
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Fig-17Fig-18Fig-19

6/12



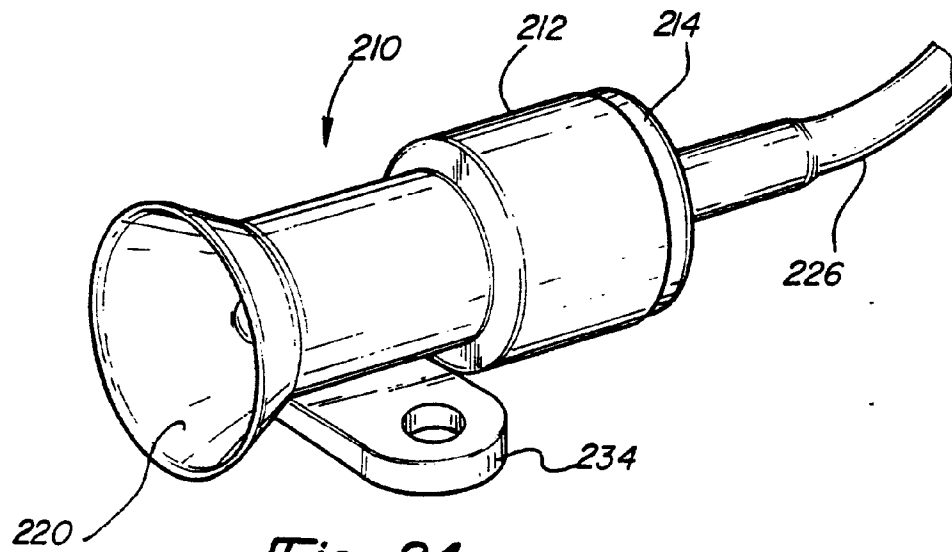


Fig-24

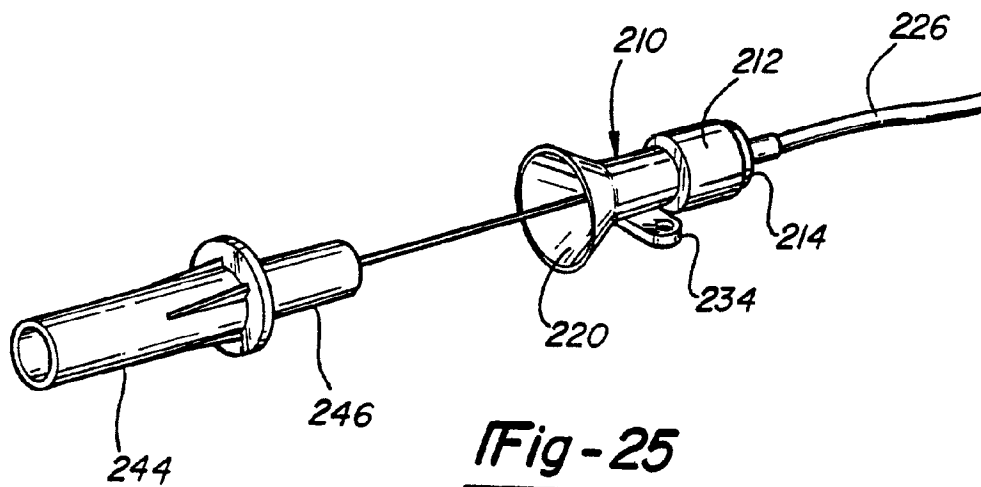
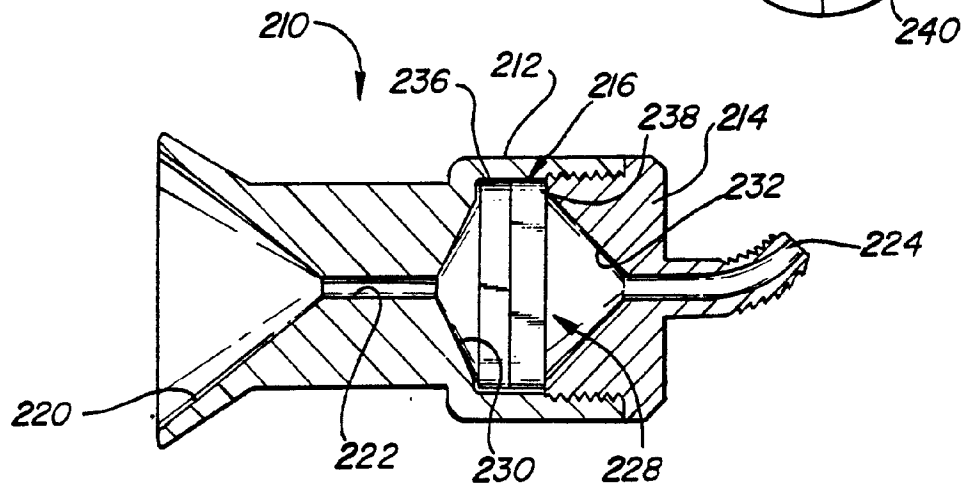
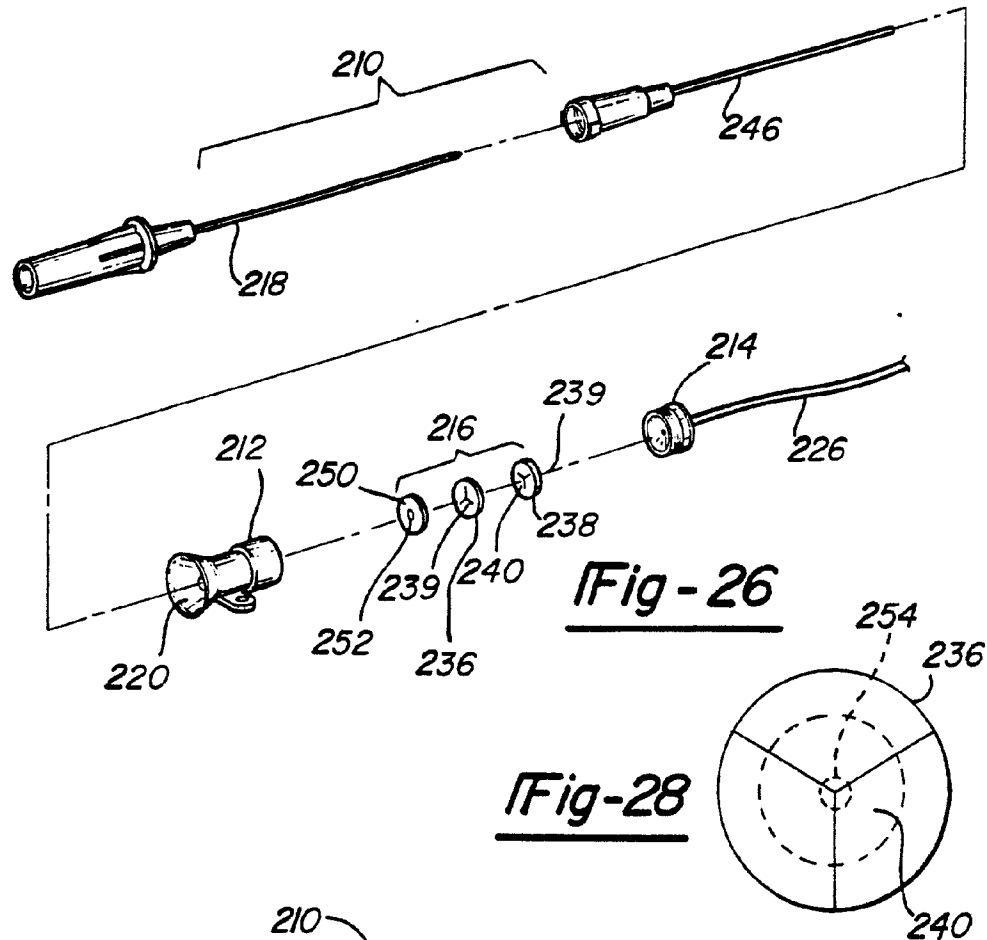


Fig-25

8/12



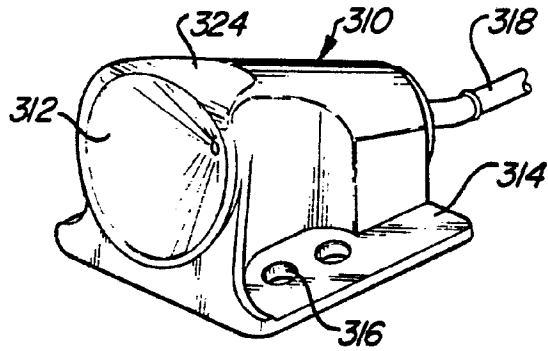


Fig-29

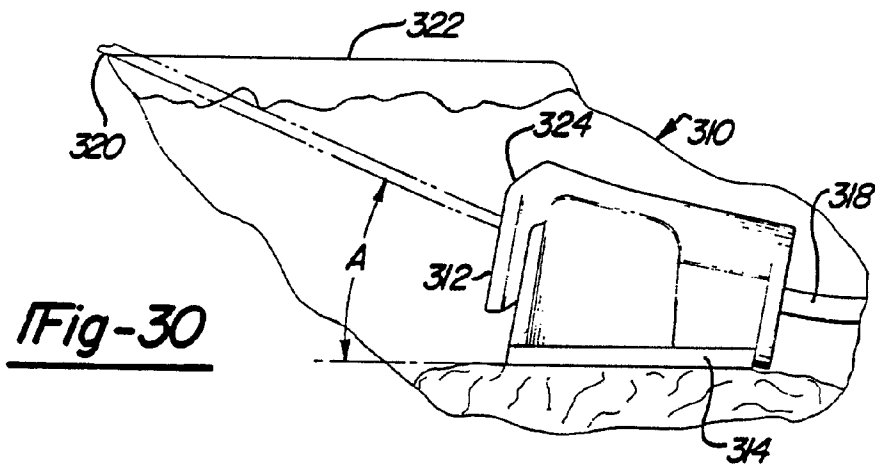


Fig-30

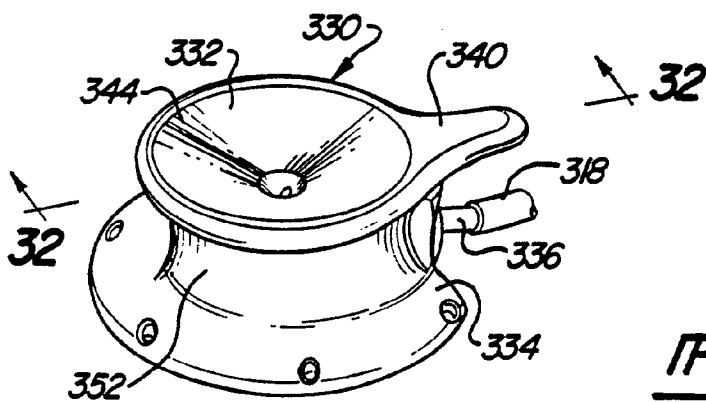
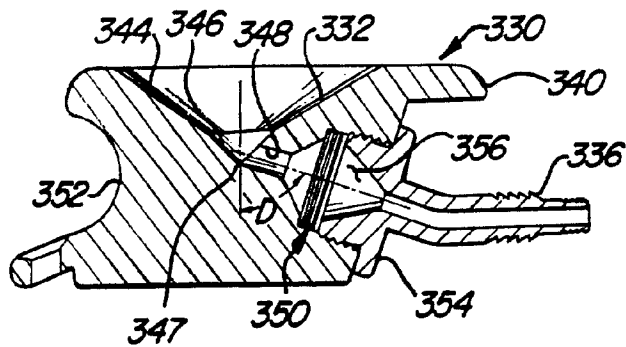
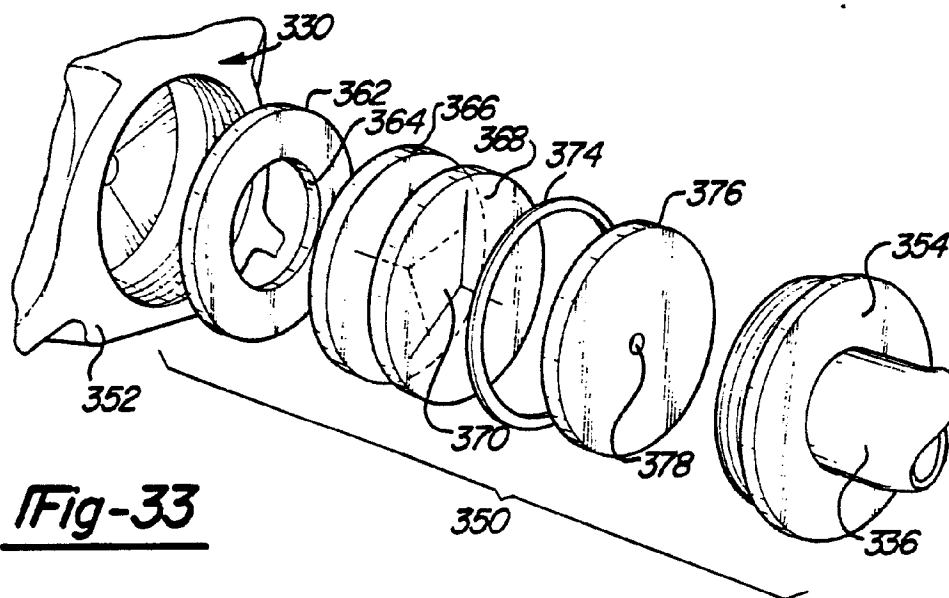
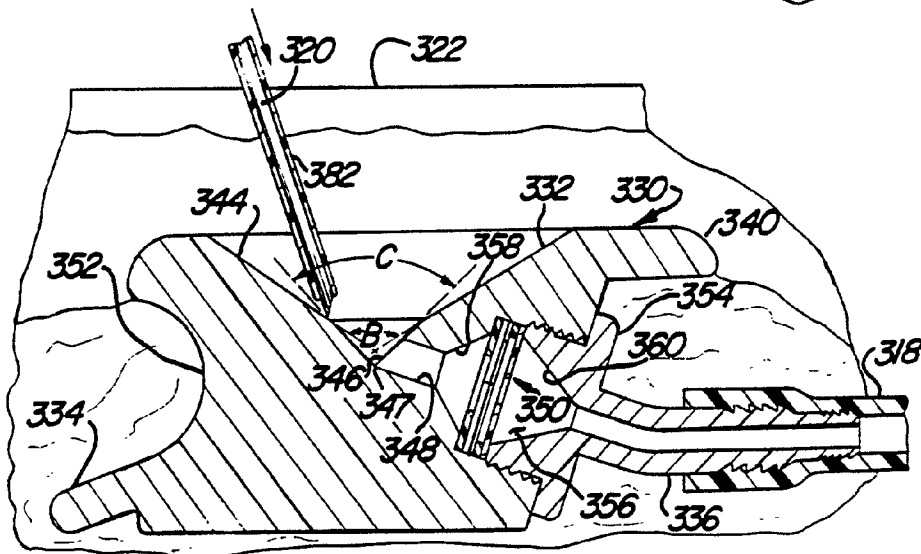
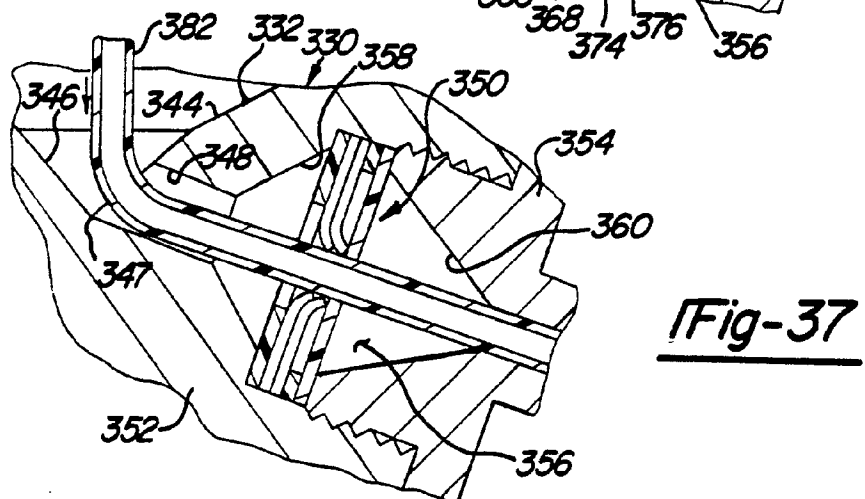
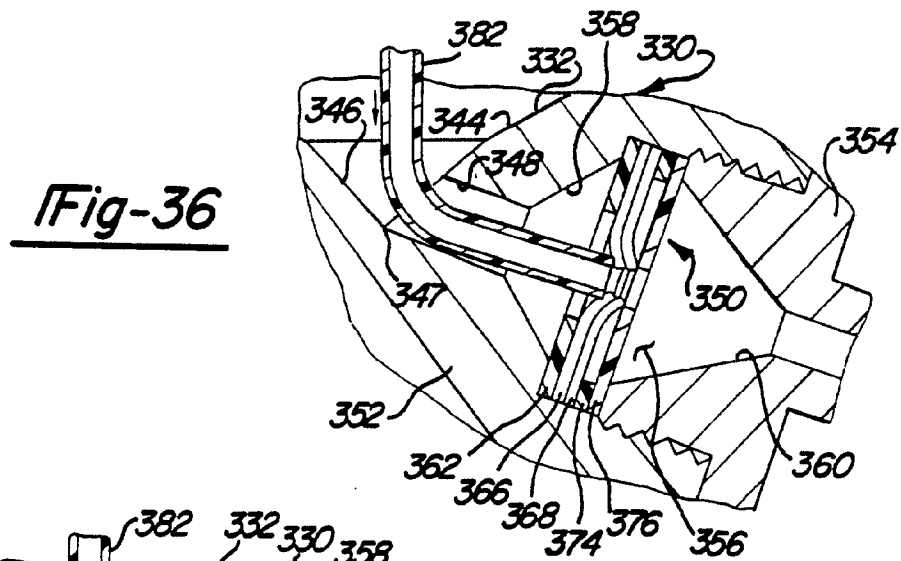
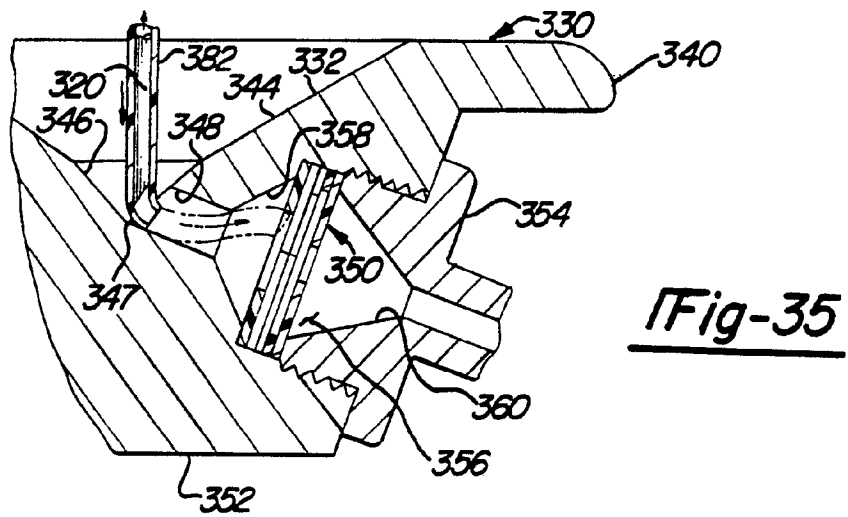


Fig-31

Fig-32Fig-33Fig-34



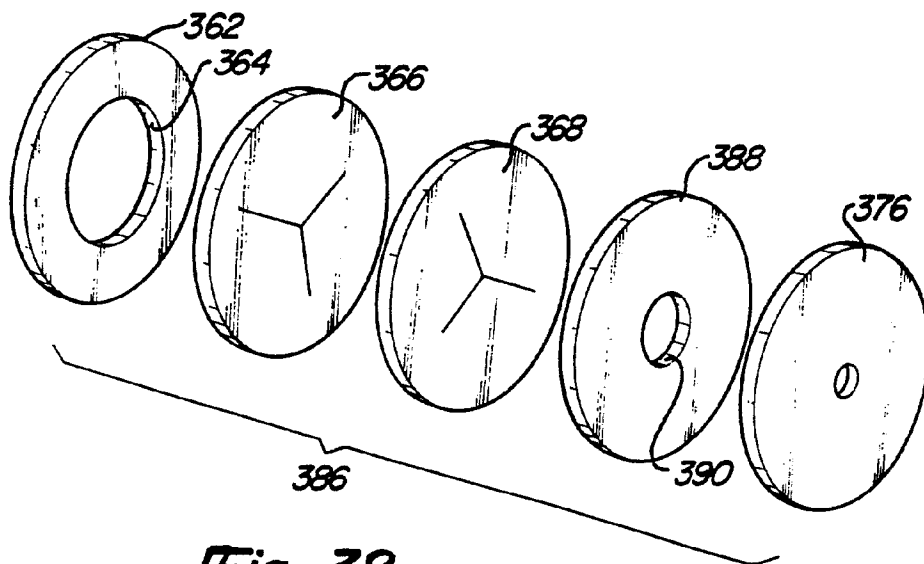


Fig-38

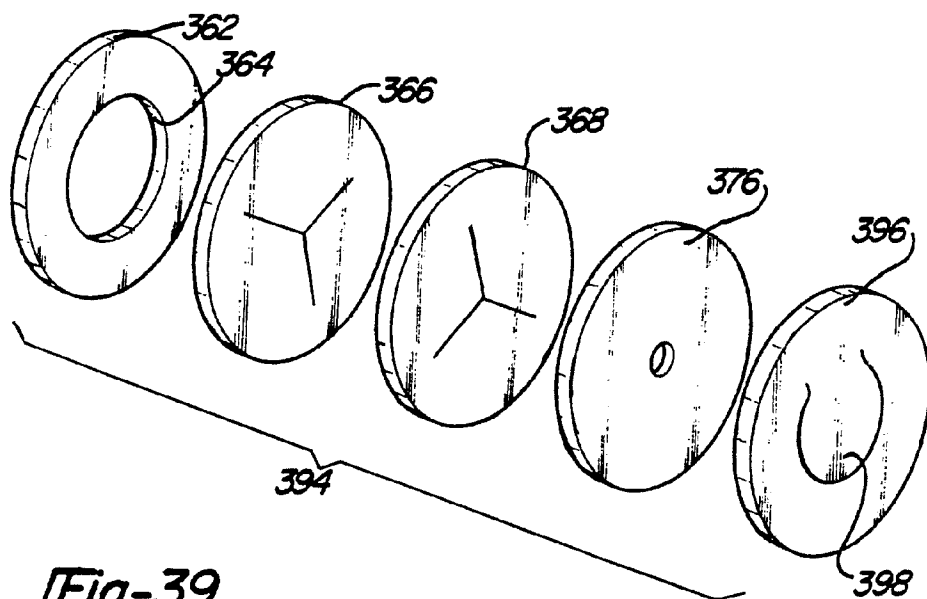


Fig-39

INTERNATIONAL SEARCH REPORT

International Application No. PCT/US91/01414

I. CLASSIFICATION OF SUBJECT MATTER

According to International Patent Classification (IPC) or to both National Classification and IPC

IPC(5): A61M 5/178

U.S.CL.: 604/167

II. FIELDS SEARCHED

Minimum Documentation Searched

Classification System

Classification Symbols

US

604/167,175,93,86,244,256,83,4,8,9,10,49,905

Documentation Searched other than Minimum Documentation to the extent that such Documents are included in the Fields Searched

III. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of Document, ** with indication, where appropriate, of the relevant passages **	Relevant to Claim No. **
X	US,A, 4,857,062 (RUSSELL) 15 AUGUST 1989 (SEE ENTIRE DOCUMENT)	1,2,6,9,12,13, 15,17,20-22,27
Y	US,A, 4,430,081 (TIMMERMANS) 07 FEBRUARY 1984 (SEE ENTIRE DOCUMENT)	3-5,14,16,26
A	US,A, 4,447,237 (FRISCH ET AL) 08 MAY 1984 (SEE ENTIRE DOCUMENT)	1-43
A	US,A, 4,569,675 (PROSL ET AL) 11 FEBRUARY 1986 (SEE ENTIRE DOCUMENT)	1-43
A	US,A, 4,673,394 (FENTON, JR. ET AL) 16 JUNE 1987 (SEE ENTIRE DOCUMENT)	1-43
A	US,A, 4,710,167 (LAZORTHES) 01 DECEMBER 1987 (SEE ENTIRE DOCUMENT)	1-43
A	US,A, 4,781,693 (MARTINEZ ET AL) 01 NOVEMBER 1988 (SEE ENTIRE DOCUMENT)	1-43

* Special categories of cited documents: 10

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step

"Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

IV. CERTIFICATION

Date of the Actual Completion of the International Search

21 MAY 1991

International Searching Authority

ISA/US

Date of Mailing of the International Search Report

02 JUL 1991

Signature of Authorized Officer

For

Nguyen Ngoc Ho

NGUYEN NGOC-HO

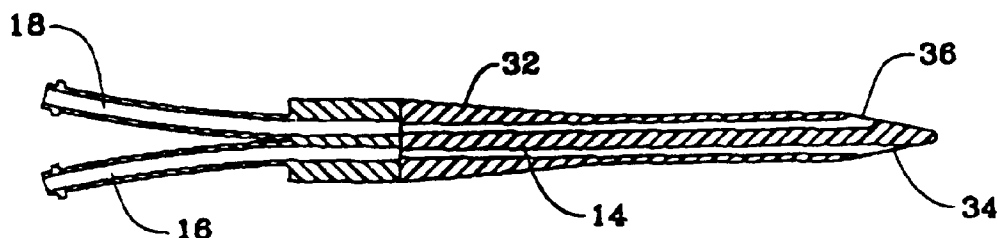
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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : A61M 3/00, 25/00	A1	(11) International Publication Number: WO 97/10858 (43) International Publication Date: 27 March 1997 (27.03.97)
(21) International Application Number: PCT/US96/14972 (22) International Filing Date: 18 September 1996 (18.09.96) (30) Priority Data: 60/004,071 21 September 1995 (21.09.95) US (71) Applicant (for all designated States except US): QUINTON INSTRUMENT COMPANY [US/US]; 3303 Monte Villa Parkway, Bothell, WA 98021 (US). (72) Inventor; and (75) Inventor/Applicant (for US only): HICKS, Allen, J. [US/US]; 14808 N.E. 201st Street, Woodinville, WA 98072 (US). (74) Agents: ALLISON, Richard, D.; Quinton Instrument Company, 3303 Monte Villa Parkway, Bothell, WA 98021 (US) et al.		(81) Designated States: AU, BB, BG, BR, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KP, KR, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, ARIPO patent (KE, LS, MW, SD, SZ, UG), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i>

(54) Title: TAPERED AND REINFORCED CATHETER**(57) Abstract**

A tapered single (50) or multi-lumen catheter (10, 70) having an elongated cylindrical tube (28) for injection and removal of fluid, is provided with generally constant or gradually increasing diameter internal lumen or lumens (16, 18) which are connected to a tip portion (26) which may be a conical tapered tip that smoothly merges with the cylindrical surface of the tube (28) so that insertion trauma and the possibility of kinking are minimized. The catheter body is generally formed of proximal and distal portions wherein the proximal portion preferably includes a portion (30) which increases in external diameter in the proximal direction to provide a strain relief for the intersection of the catheter body (12) and the hub member (20) of the catheter. The portion of the catheter body which increases in diameter may also include one or more lumens therein which similarly increase in diameter to increase the flow of fluid therethrough or which are of constant diameter such that the outer wall (32) of the catheter body increases in thickness therealong to increase the columnar strength of the catheter body therealong.

TAPERED AND REINFORCED CATHETER**TECHNICAL FIELD**

The present invention relates to surgical instruments for withdrawing fluids from or introducing fluids into a cavity of the body such as through multi-lumen catheters for use in extracorporeal or other medical procedures.

BACKGROUND ART

As is well known, a catheter is a tubular, flexible, surgical instrument for withdrawing fluids from (or introducing fluids into) a cavity of the body. A double-lumen catheter is a catheter having two lumens--one for injection and one for removal of fluid or both lumens for either injection or fluid removal as needed. As is well known, a double-lumen catheter may be used for removing blood from a fistula or vein for processing in a dialysis machine and returning the processed blood back to the fistula or vein. A double-lumen catheter suitable for this purpose is disclosed in Mahurkar, U.S. Patent No. 4,134,402 issued January 16, 1979. Mahurkar U.S. Patent No. 4,134,402 discloses a double lumen continuous flow hemodialysis needle and cannula having contiguous lumens of different lengths formed by dividing a unitary straight tube, the shorter lumen acting as a blood intake lumen and the longer acting as a blood return lumen. Semicircular lumens provide a minimal resistance to blood flow resulting in a smaller but highly efficient catheter in comparison to a coaxial double-current catheter. Hemodialysis requires, for example, a blood flow rate of about 200 ml/min. or more and flow resistance less than about 100 mm of mercury.

Mahurkar, U.S. Patent No. Des. 272,651 issued February 14, 1984, discloses a double lumen catheter having an outlet lumen which has an opening at the tip of the catheter and a shorter inlet lumen which terminates in a bevel substantially displaced from the tip.

Mahurkar, U.S. Patent No. 4,583,968 issued April 22, 1986, discloses a double lumen catheter having an outlet lumen which has an opening at the tip of the smooth conical tip member and a shorter inlet lumen which terminates proximally of the tip member. Additionally, the use of a coaxial sleeve at the junction of the tube and the connector is disclosed to provide a strain relief and reduce the likelihood of kinking at the junction.

There are numerous other United States patents disclosing double or multi-lumen catheters for hemodialysis other procedures and evidencing a long-felt need for a small, functionally efficient catheter having a minimum of insertion trauma and potential for clotting and kinking.

The catheters described above are generally directed to the use of a straight cylindrical tube which may be subject to occasional kinking because the portion of the cylindrical tube exiting the body of the patient has the same structural strength as the other portions along the length of the cylindrical tube. Additionally, the diameter of the internal lumens are also generally kept constant throughout the length of the cylindrical tube to maintain a constant flow pressure, although one form of the present invention maintains the thickness of the outer wall of the catheter constant while increasing the outer diameter of the catheter and the diameter of the internal lumens as described below.

It is therefore desirable to provide an improved catheter which includes a tapered portion generally along the proximal portion of the catheter body to form a strain relief area therealong. Additionally, it is also desirable to provide an improved catheter having one or more internal

lumens with a diameter that is greater along the proximal portion of the catheter body than the distal portion of the catheter body to provide reduced pressures while providing increased flows in as small a catheter as possible.

5

DISCLOSURE OF THE INVENTION

The primary object of the invention is to provide an efficient single or multi-lumen catheter having minimal insertion trauma and a minimal potential for clotting and kinking.

10

Another object of the invention is to provide a single or multi-lumen catheter which is an effective dilator for soft tissue and veins and which minimizes kinking during insertion and use.

15

Yet another object of the invention is to provide a dual lumen catheter which utilizes hub and extension tubing components from a larger diameter catheter to minimize the need to stock multiple sizes of parts for various size catheters while providing the further advantage of minimizing kinking during use.

20

In accordance with one form of the invention, a dual lumen catheter has a pair of lumens with constant internal diameters while the proximal portion of the catheter body gradually increases in thickness as it approaches the hub member of the catheter to increase the tubular stiffness or columnar strength of the proximal portion of the catheter body. The increased thickness of the material in the walls of the proximal portion of the catheter body increases the columnar strength of the catheter adjacent to hub member of the catheter to form a strain relief area so that the likelihood that the catheter will kink at the intersection of the catheter body and hub member is minimized. Additionally, the gradually increasing external diameter along the proximal portion of the catheter body

25
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exponentially strengthens the portion of the catheter body which exits from the body of the patient to minimize kinking at this location also. The present invention also allows the same hub members to be used for small diameter catheters as are used for larger diameter catheters. This feature further decreases the resistance to fluid flow typically present through the extension members and hub member by providing a proportionally larger internal diameter in the hub member and extension members than in the catheter body while also allowing for the lower cost manufacture of the relatively low sales volume smaller catheters by using components which are common to the larger sales volume catheters.

Another effect of the present invention relates to the embodiment which includes tapered lumens along the proximal portion thereof. By tapering the internal lumen of the proximal portion of the catheter body, the volume of fluid or blood that is passed through the catheter body is increased at reduced pressures while still providing the catheter strain relief effect described above. This effect is explained by Pouiseuille's equation for flow within a tube where $V = p(d)^4 / n l$. In this equation, V = flow, p = pressure, d = tube diameter, n = viscosity and l = length of the tube. Therefore, the ratio of pressure is dependent not only upon the diameter of the tube, but also in a 1:1 ratio with the length of the tube and as the diameter of the internal lumen is increased, the pressure is decreased and the flow increases in proportion to the length of tube having the increased diameter of the internal lumen.

In accordance with one form of the invention, the dual lumen catheter may also have a smooth conical tapered tip that smoothly merges with the distal portion of the catheter body so that insertion of the catheter is facilitated. The conical tip forms a tip guidance point which is located at the center of the conical tip for uniform distribution of frictional resistance and while

minimizing insertion trauma and kinking. The conical tapered tip comprises a relative concentration of material to impart relative rigidity so that the tip functions as an effective dilator for soft tissue and veins. Semicircular lumens may also be provided to insure non-static laminar flow and prevent clotting. A double lumen catheter of this type may be particularly advantageous when a tunneling procedure or blind technique must be used, for example, to reach a vein under the collar bone or neck.

In accordance with the present invention, the catheter may also have a single or plural lumens and may increase in external diameter from the approximate lengthwise middle of the catheter body. Additionally, as described above, in one form of the present invention, the diameter of the internal lumen or lumens of the catheter body may increase proportionally with the increased external diameter of the proximal portion of the catheter body so that the wall thickness remains the same or is increased slightly as the intersection with the hub member is reached.

BRIEF DESCRIPTION OF THE DRAWINGS

Other objects and advantages of the invention will become apparent from the following detailed description and the accompanying drawings, in which:

Figure 1 is a front elevational view of a double lumen catheter according to the present invention;

Figure 2 is a right side elevational view of the double lumen catheter illustrated in Figure 1;

Figure 3 is a view in section of the double lumen catheter illustrated in Figure 1 taken along line 3-3 thereof; Figure 4 is a view in section of the double lumen catheter illustrated in Figure 1 taken along line 4-4 thereof; Figure 5 is a view in section of the double lumen

catheter illustrated in Figure 1 taken along line 5-5 thereof;

Figure 6 is a view in section of the double lumen catheter illustrated in Figure 1 taken along line 6-6 shown
5 in Figure 2;

Figure 7 is a front elevational view of a single lumen catheter according to the present invention;

Figure 8 is a view in section of the single lumen catheter illustrated in Figure 7 taken along line 8-8
10 thereof; Figure 9 is a view in section of the single lumen catheter illustrated in Figure 7 taken along line 9-9 thereof; Figure 10 is a view in section of the single lumen catheter illustrated in Figure 7 taken along line 10-10 thereof;

Figure 11 is a view in section of the single lumen catheter illustrated in Figure 7 taken along line 11-11
15 shown in Figure 7;

Figure 12 is a front elevational view of a triple lumen catheter according to the present invention;

Figure 13 is a view in section of the triple lumen catheter illustrated in Figure 12 taken along line 13-13
20 thereof;

Figure 14 is a view in section of the triple lumen catheter illustrated in Figure 12 taken along line 14-14
25 thereof;

Figure 15 is a view in section of the triple lumen catheter illustrated in Figure 12 taken along line 15-15 thereof;

Figure 16 is a view in section of the triple lumen catheter illustrated in Figure 12 taken along line 16-16
30 shown in Figure 12;

Figures 17, 18 and 19 are views in section showing an alternate cross sectional configuration in a double lumen catheter of the type shown in Figure 1 wherein Figures 17,
35 18 and 19 are cross sectional configurations taken

generally along the same lines as lines 3-3, 4-4 and 5-5 of Figure 1; and

Figure 20 is a front elevational view of an alternate form of a double lumen catheter according to the present invention.

While the invention will be described in connection with a certain preferred embodiment, it will be understood that it is not intended to limit the invention to that particular embodiment. On the contrary, it is intended to cover all alternatives, modifications, and equivalents as may be included within the spirit and scope of the invention as defined by the appended claims.

BEST MODE FOR CARRYING OUT THE INVENTION

Turning now to the drawings, Figures 1-20 show various embodiments of the catheters of the present invention, generally designated as 10, 50 and 70, respectively. As is conventional for a double lumen catheter 10 has an elongated hollow tube or catheter body 12 which is inserted into a cavity of the body such as a fistula or vein. The catheter body 12 is preferably circular in external cross section, as specifically shown in Figures 3-5, and has an internal septum 14 defining a return lumen 16 and an inlet lumen 18 within the interior of the catheter body 12. The lumens 14 and 16 of the embodiment shown in Figures 1-6 are have a constant diameter and are preferably semicircular or "D" shaped to minimize the resistance to fluid flow. As is conventional for this type of dual lumen construction, the septum 14 extends axially along the catheter body 12 from a hub member 20. The hub member 20 connects the proximal end portions of catheter body 12 including the return lumen 14 and the inlet lumen 16 to respective fluid return and inlet extensions 22 and 24 which are, for example, respective venous and arterial lines or extension members

which are connected to a dialysis or similar unit. The proximal side of the hub member 20 connects to the return extension 22 and inlet extension 24 which are then connected to the dialysis or other machine. The preferred
5 direction of fluid circulation when the present invention is used for extra corporeal procedures such as hemodialysis, apherisis or similar applications is indicated by the arrows in Figure 1.

As best shown in Figure 6, the catheter body 12
10 generally includes a tip portion 26 which is connected to the distal end of the distal portion 28 of the catheter body 12 and a proximal portion 30 which is connected to the distal side of the hub member 20. The diameters of the return and inlet lumens, 16 and 18, are preferably
15 maintained constant along the lengthwise dimension of the catheter body 12 in this embodiment while the thickness of the outer wall 32 of the catheter body 12 is increased. This increase in the thickness of the outer wall 32 provides a strain relief along the proximal portion 30 of
20 the catheter body 12 and is illustrated by comparing Figures 3, 4 and 5. Alternately, the diameter of the outer wall 32 may also be increased while maintaining the thickness of the outer wall 32 constant so that the diameter of the return lumen 16 and inlet lumen 18 along
25 the proximal portion 30 of the catheter body 30 are also increased as shown in Figure 20 to decrease the resistance to the flow of fluid therethrough. This feature, in addition to the ability to use a hub member and extension members having larger internal diameters provides a
30 catheter having an increased flow of fluids while the resistance to the flow of fluids therethrough is reduced.

The distal portion 28 of the catheter body 12 includes openings or apertures at the distal end portions of the lumens to permit the flow of fluid between a body cavity
35 (not shown) and the lumens. The return lumen 16 extends along the entire length of the catheter body 12 to an

aperture or opening 34 at the distal end or tip portion 26 of the catheter 10. The inlet lumen 18 is shorter than the return lumen 16 and terminates at its distal end at an aperture or opening 36 that is in the outer wall 32 of the catheter body 12 and is displaced from the opening 34 at the distal end of the catheter 10.

In accordance with a preferred form of the invention, the catheter body 12 is connected to a conical tip portion 26 which smoothly merges with the catheter body 12 at the intersection thereof. Preferably, the apex of the tip portion 26 of this embodiment is centered on the axis of the catheter body 12 of the catheter 10 thus serving as a guidance point to uniformly distribute the frictional resistance encountered by the tip portion 26 when the catheter 10 is inserted into the body cavity (not shown). As shown in Figures 1 and Figure 6, the outer diameter of the distal portion 28 of the catheter body 12 of the catheter 10 converges smoothly at the intersection of the distal portion 28 and the tip portion 26 to form a truncated cone and the return lumen 16 opens at the truncated apex of the cone. As shown, the tip portion 26 of this embodiment preferably has a gradual taper which preferably has a length of approximately two or more diameters of the catheter body 12. Since the frictional resistance to insertion is uniformly distributed and the tip portion 26 smoothly merges with the distal portion 28 of the catheter body 12, insertion trauma and kinking are minimized. The tip portion 26 may also be formed as a blunt tip where the return and inlet lumens open at the same location or a staggered tip where the inlet lumen 18 opens along the lengthwise dimension of the catheter body 12 and the remaining portion of the catheter body 12 distally of the inlet lumen 18 is generally circular and is smaller than the diameter of the portion of the catheter body 12 surrounding the inlet lumen 18 and the return lumen 16.

The conventional use of relatively small return openings 34 and inlet openings 36 also function to reduce insertion trauma, but they also impede fluid flow. Therefore, an additional group of holes or apertures may be used to connect the return lumen 22 to the outer surface of the catheter body 12, and an additional group of holes or apertures may be used to connect the inlet lumen 18 to the outer surface of the catheter body 12. The return holes or apertures may be axially disposed between the base of the tip portion 26 and the inlet aperture 34 at the distal end of the inlet lumen 18. The additional inlet holes or apertures may be axially disposed between the inlet aperture 36 and the proximal end of the catheter body 12. The return holes and the inlet holes are further disposed circumferentially on opposite sides of the septum 14. Thus, there is axial as well as circumferential separation of the inlets and outlets for fluid circulation. Alternately, either or both of the inlet holes and return holes of the present invention may be formed as an elongate slot of the type disclosed in U.S. Patent No. 5,403,291 wherein the opening may be shaped generally as a parallelogram on the outer wall 32 of the catheter body 12.

As shown in Figure 6, the tip portion 26 is generally formed with a relatively large concentration of material to provide increased stiffness to the tip portion 26. This stiffening aids penetration of the tip portion 26 into the body cavity (not shown) and also aids the dilation of soft tissue such as veins. The tip portion 26 as shown in Figure 6 is preferably formed from a material such as a thermo-plastic material. The tip portion 26 including the relative concentration of material is readily molded and bonded or is integrally formed from the cylindrical catheter body 12 by the use of internal and external mandrels and the application of heat by any number of conventional means such as RF forming, thermal forming or infrared forming.

For use in hemodialysis type procedures, the double lumen catheter 10 is introduced in the direction of blood flow in a large vein over a hypodermic needle or Seldinger's guide wire, or through a sheath as is conventional. The side opening 36 on the blood inlet lumen 18 draws the blood for processing by a hemodialysis, apheresis or similar machine and the processed blood is returned through the return lumen 16 and out through the opening 34 to return the blood upstream into circulation. The geometrical properties of the double lumen catheter as shown in the drawing figures insure that insertion trauma, kinking, and the possibility of clotting are minimized during use including hemodialysis procedures.

As shown in Figures 7-11, the catheter 50 of this alternate embodiment is a single lumen catheter having a catheter body 52 which is preferably circular in external cross section, as specifically shown in Figures 8-10. The lumen 54 of the embodiment shown in Figures 7-11 has a generally constant diameter and is shaped to minimize the resistance to fluid flow. As is conventional for this type of single lumen catheter, the catheter body 52 extends between a hub member 56 and the tip portion 58. The hub member 56 connects the proximal end portion of catheter body 52 and includes an extension member 64 which may then be connected to an external device or unit.

As best shown in Figure 11, the catheter body 52 generally includes the tip portion 58 which is connected to the distal end of a distal portion 60 of the catheter body 52 and a proximal portion 62 which connected to the distal side of the hub member 56. In this embodiment, the diameter of the lumen 54 is preferably maintained generally constant along the lengthwise dimension of the catheter body 52 while the thickness of the outer wall 66 of the catheter body 52 is increased. This increase in the thickness of the outer wall 66 provides a strain relief along the proximal portion 62 of the catheter body 52 and

is illustrated by comparing Figures 8, 9 and 10. Alternately, the diameter of the outer wall 66 may be increased while maintaining the thickness of the outer wall 66 constant so that the diameter of the lumen 54 is also increased in the manner shown in the embodiment of Figure 20. Additionally, although the tip portion 58 of this embodiment is shown as being generally conical, blunt or staggered tip portions as described above may also be used with the present embodiment.

As shown in Figures 12-16, the catheter 70 of this alternate embodiment is a triple lumen catheter having a catheter body 72 which is preferably circular in external cross section, as specifically shown in Figures 13-15. The lumens 74, 76, and 78 of the embodiment shown in Figures 12-16 also have a generally constant diameter with an outer wall 80 which gradually increases in thickness proximally along the proximal portion 82 of the catheter body 72 and are shaped to minimize the resistance to fluid flow therethrough.

The catheter body 72 of this embodiment is preferably circular in external cross section, as shown in Figures 13-15, and has an internal septum 84 defining first, second and third lumens, 74, 76, and 78 respectively, within the interior of the catheter body 72. The lumens 74, 76 and 78 of the embodiment shown in Figures 12-16 preferably have a constant diameter and the first lumen 74 and second lumen 76 are preferably larger in diameter than the third lumen 78 and are generally semicircular or "D" shaped to minimize the resistance to fluid flow therethrough. As is conventional for this type of triple lumen catheter 70, the septum 84 extends axially along the catheter body 72 from a hub member 86 to a tip portion 88 on the distal portion 90 of the catheter body 72. The hub member 86 securely connects the proximal portion 82 of catheter body 72 including the first, second and third lumens 84, 86 and 88 to respective extensions members 92, 94 and 96 which are in

flow communication with their respective lumens through the hub member 86. The proximal side of the hub member is connected to the extension members 92, 94 and 96 which are then connected to the external unit or device.

5 As best shown in Figure 16, the catheter body 72 generally includes a tip portion 98 which is connected to the distal end of the distal portion 90 of the catheter body 72 and a proximal portion 82 which is connected to the distal side of the hub member 86. The diameter of the
10 respective lumens, 74, 76 and 78, are preferably maintained constant along the lengthwise dimension of the catheter body 72 in this embodiment while the thickness of the outer wall 80 of the catheter body 72 is increased. This increase in the thickness of the outer wall 80 provides a
15 strain relief along the proximal portion 82 of the catheter body 72 to resist bending or kinking along the intersection of the catheter body 72 and the hub member 86 and is illustrated by comparing Figures 13, 14 and 15. Alternately, the diameter of the outer wall 80 may be
20 increased while maintaining the thickness of the outer wall 80 constant so that the diameter of the first, second and/or third lumens may be increased as desired generally in the manner shown in Figure 18.

The distal portion 90 of the catheter body 72 of this
25 embodiment includes openings or apertures at the distal end portions of the lumens to permit the flow of fluid between a body cavity (not shown) and the lumens. The first lumen 74 extends along the entire length of the catheter body 72 to an aperture or opening 100 at the distal end or tip
30 portion 88 of the catheter 70. The second lumen 76 is preferably shorter than the first lumen 74 and terminates at its distal end at an aperture or opening 102 that is in the outer wall 80 of the catheter body 72 and is displaced proximally from the opening 100 at the distal end of the
35 catheter 70. The third lumen 78 is preferably shorter than the first lumen 74 and the second lumen 76 and preferably

terminates at its distal end at an aperture or opening 104 that is in the outer wall 80 of the catheter body 72. The opening for the third lumen 78 is preferably displaced proximally and axially from the opening 102 of the second
5 lumen 76.

Figures 17, 18 and 19 are illustrative of a dual lumen catheter which is similar in side view to the catheter shown in Figure 1 and therefore, like numbers have been added to like members. The catheter body 12 of this
10 embodiment is preferably circular in external cross section and has an internal septum 14 defining a return lumen 16 and an inlet lumen 18 within the interior of the catheter body 12. The lumens 14 and 16 of the embodiment shown in Figures 17-19 preferably have a constant diameter and are
15 preferably shaped to include a generally circular return lumen 16 and an oblong or tear drop shaped inlet lumen 18. As is conventional for this type of dual lumen construction, the septum 14 extends axially along the catheter body 12 from a hub member (not shown). The hub
20 member connects the proximal end portions of catheter body 12 including the return lumen 14 and the inlet lumen 16 to respective fluid return and inlet extensions (not shown) which are, for example, respective venous and arterial lines or extension members which are connected to a
25 dialysis or similar unit. The proximal side of the hub member connects to the return extension and inlet extension which are then connected to the dialysis or other external machine or device.

The diameter of the return and inlet lumens, 16 and
30 18, of this embodiment is preferably maintained constant along the lengthwise dimension of the catheter body 12 while the thickness of the outer wall 32 of the catheter body 12 is increased. This increase in the thickness of the outer wall 32 provides a strain relief along the
35 proximal portion 30 of the catheter body 12 and is illustrated by comparing Figures 17, 18 and 19.

Alternately, the diameter of the outer wall 32 may be increased while maintaining the thickness of the outer wall 32 constant so that the diameter of the return lumen 16 and inlet lumen 18 along the proximal portion 30 of the catheter body 30 are also increased as shown in Figure 20 to provide a decrease in the resistance to the flow of fluid therethrough.

CLAIMS

What is claimed is:

1. A catheter comprising an elongated cylindrical tube having a longitudinal interior lumen, said tube having distal and proximal portions and a tip member on the distal end of said distal portion and said proximal portion of
5 said cylindrical tube connecting to a hub member and said hub member connecting to at least one separate extension member and said at least one extension member communicating with said lumen via said hub member for the injection and removal of fluid through said cylindrical tube, said
10 cylindrical tube having an external diameter wherein said diameter of said distal portion is generally uniform and said diameter of said proximal portion increases in diameter in the proximal direction thereof such that said diameter of said cylindrical tube is greater adjacent to
15 said hub member than said diameter of said distal portion.
2. The catheter of claim 1, wherein said lumen of said cylindrical tube includes a diameter which is generally uniform throughout the lengthwise dimension thereof.
3. The catheter of claim 1, wherein said cylindrical tube includes a diameter which is greater adjacent to said hub member than said diameter of said lumen in said distal portion of said cylindrical tube.

4. The catheter of claim 1, wherein said cylindrical tube includes at least one septum extending longitudinally therethrough to form a plurality of lumens therein and said lumens each having a diameter which is generally uniform
5 throughout the lengthwise dimension thereof.

5. The catheter of claim 1, wherein said cylindrical tube includes at least one septum extending longitudinally therethrough to form a plurality of lumens therein and said lumens each having a diameter which is greater adjacent to
5 said hub member than said diameter of said lumens in said distal portion of said cylindrical tube.

6. The catheter of claim 1, wherein said tip member includes a conical tapered tip member having a concentration of material exceeding the concentration of material in the cylindrical body of said cylindrical tube.

7. The catheter of claim 1, wherein said cylindrical tube includes first and second lumens therein and said first lumen extends lengthwise along said cylindrical tube and said tip member and said second lumen terminates at an
5 opening in the side of said cylindrical tube.

8. The catheter of claim 1, wherein said tip member includes an apex thereon and said apex of said tip member is substantially aligned with the axis of said cylindrical tube.

9. The catheter of claim 1, wherein the length of said tip member is at least approximately two diameters of said cylindrical tube.

10. The catheter of claim 1, wherein said cylindrical tube includes first and second lumens therein and said first and second lumens are of semicircular cross sectional shape.

11. The catheter of claim 1, wherein said cylindrical tube includes first and second lumens therein and said first and second lumens are of different cross sectional shape.

12. A multiple lumen catheter comprising an elongated cylindrical tube including an axial divider bisecting said cylindrical tube into first and second lumens and including proximal and distal portions thereof and said proximal
5 portion is connected to a hub member and said distal portion is connected to a tip member, said proximal end of said proximal portion of said cylindrical tube connecting two separate extension members communicating with the respective first and second lumens via said hub member for
10 the injection and removal of fluid, said first lumen extending from said proximal portion of said cylindrical tube to a first opening at the distal end of said distal portion of said cylindrical tube, said second lumen extending from the proximal portion of said cylindrical
15 tube to a second opening in the side of said cylindrical tube, said second lumen terminating at said second opening and said cylindrical tube having a diameter adjacent to said hub member which is greater than the diameter of said cylindrical tube along said distal portion thereof.

13. The double lumen catheter of claim 12, wherein said first lumen has a diameter which is generally uniform along the length thereof.

14. The double lumen catheter of claim 12, wherein said second lumen has a diameter which is greater adjacent to the hub member than the diameter along the length of said distal portion.

15. The double lumen catheter of claim 12, wherein said first lumen and said second lumen have a diameter which is generally uniform along the length of said cylindrical tube.

16. The double lumen catheter of claim 12, wherein said first lumen and said second lumen have a diameter which is greater adjacent to the hub member than the diameter along the length of said distal portion.

17. The double lumen catheter of claim 12, wherein said tip member is generally conical and includes a length which is at least approximately two diameters of said cylindrical tube.

18. The double lumen catheter of claim 12, wherein said second lumen opens at an opening in the side of said cylindrical tube and said tip member includes said first lumen extending therethrough.

19. The double lumen catheter of claim 12, wherein the diameter of said first lumen gradually increases in the proximal direction from the intersection of said distal portion and said proximal portion of said cylindrical tube to the intersection of said proximal portion and said hub member.

20. The double lumen catheter of claim 19, wherein the thickness of said cylindrical tube is generally uniform.

21. The double lumen catheter of claim 12, wherein the diameter of said first lumen along said distal portion is generally uniform.

22. A double lumen catheter comprising an elongated unitary cylindrical tube having distal and proximal portions and including an integral septum extending axially along the entire length of the tube and dividing the interior of said tube into a first and second lumen, the outer circumference of said tube is generally uniform along said distal portion thereof and gradually increasing in the proximal direction from the intersection of said distal portion and said proximal portion and said distal portion including a distal end having a tip member thereon and said proximal portion having a hub member thereon and said hub member having a plurality of lumens therein in fluid flow communication with said first and second lumens of said cylindrical tube.

23. The double lumen catheter of claim 22, wherein said first lumen includes a first diameter adjacent to said hub member and a second diameter along said distal portion of said cylindrical tube and said first diameter is greater than said second diameter.

24. The double lumen catheter of claim 22, wherein said cylindrical tube includes a outer wall having a generally uniform thickness along the entire length thereof.

25. A double lumen catheter comprising an elongated unitary cylindrical tube having distal and proximal portions and including an integral septum extending axially along the entire length of the tube and dividing the interior of said tube into a first and second lumen and the diameter of said first lumen is generally uniform along

said distal portion of said cylindrical tube and gradually increasing in the proximal direction from the intersection of said distal portion and said proximal portion of said
10 cylindrical tube and said distal portion including a distal end having a tip member thereon and said proximal portion having a hub member thereon and said hub member having a plurality of lumens therein in fluid flow communication with said first and second lumens of said cylindrical tube.

26. The double lumen catheter of claim 25, wherein said cylindrical tube includes a first diameter adjacent to said hub member and a second diameter along said distal portion of said cylindrical tube and said first diameter is
5 greater than said second diameter.

27. The double lumen catheter of claim 25, wherein said cylindrical tube includes a outer wall having a generally uniform thickness along the entire length thereof.

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FIG. 1

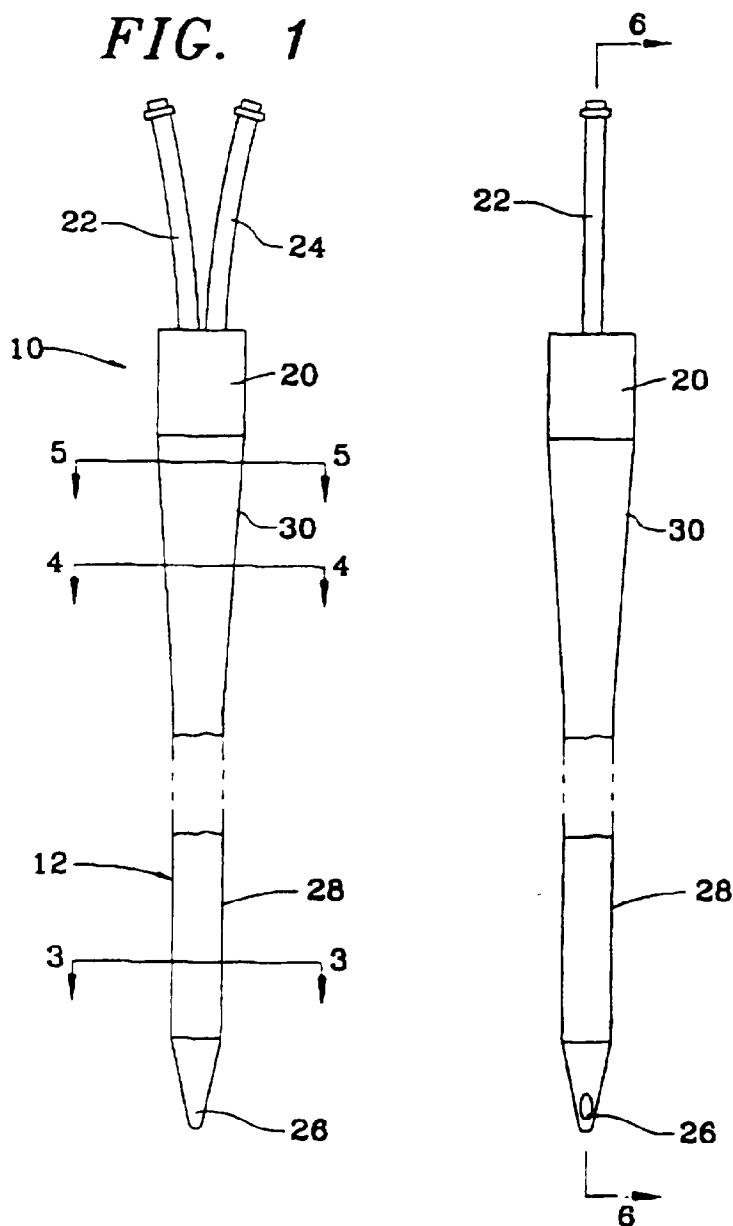


FIG. 3

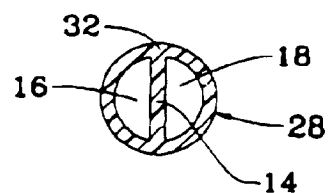


FIG. 4

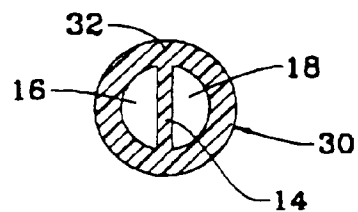


FIG. 5

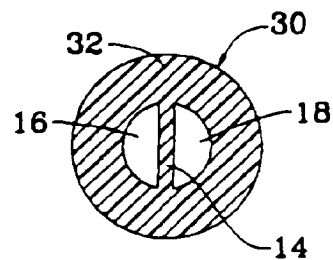
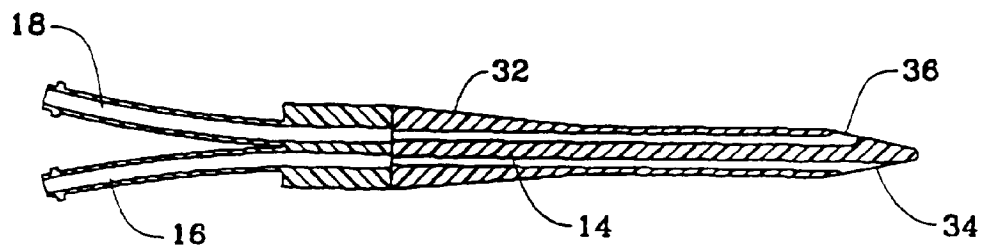


FIG. 6



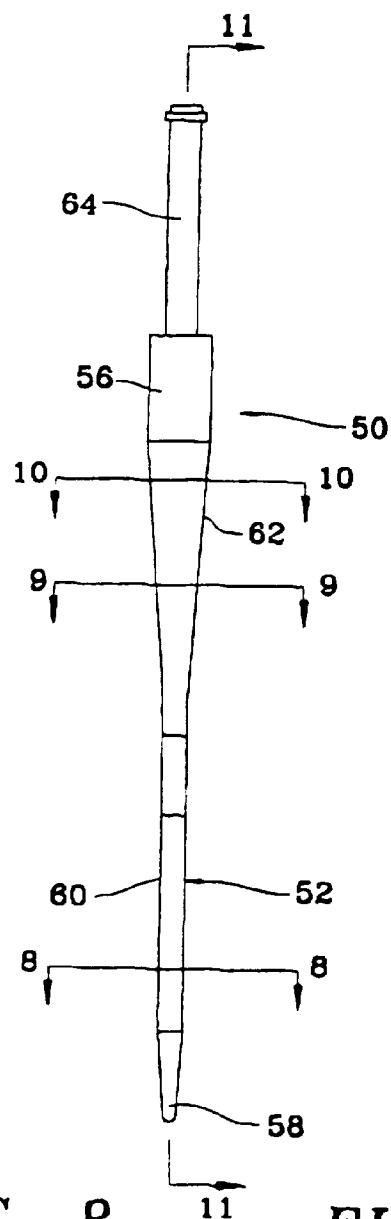


FIG. 8

FIG. 9

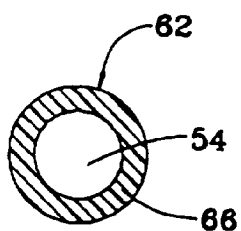
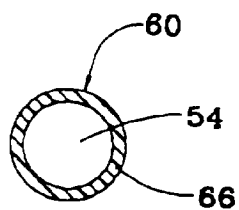


FIG. 10

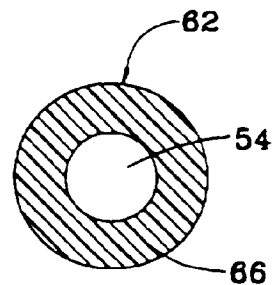
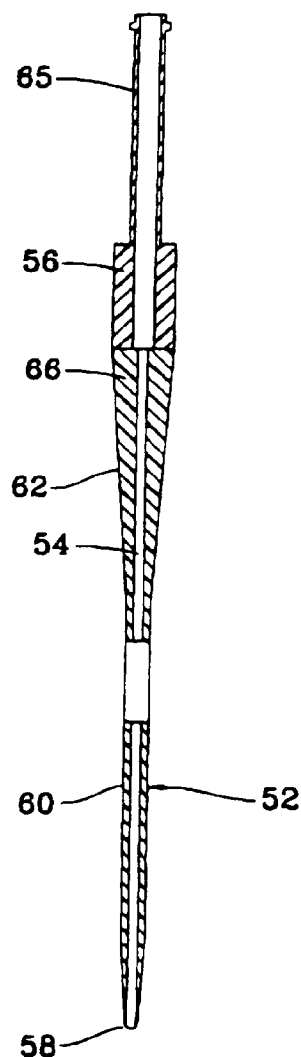


FIG. 11



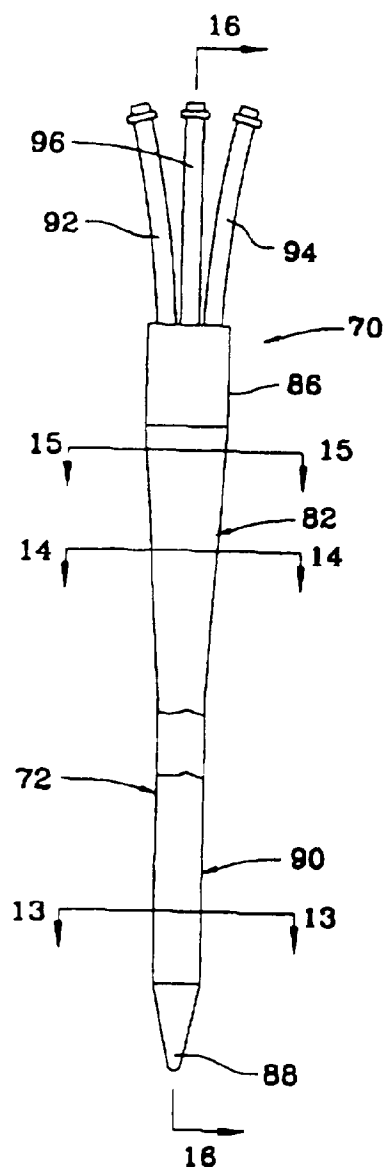


FIG. 16

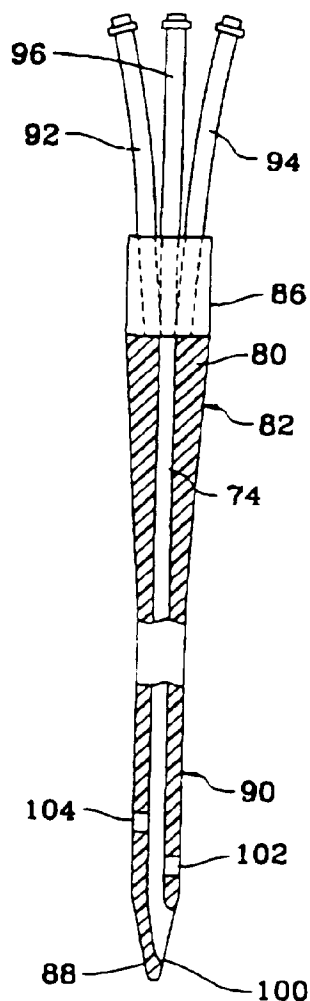


FIG. 13

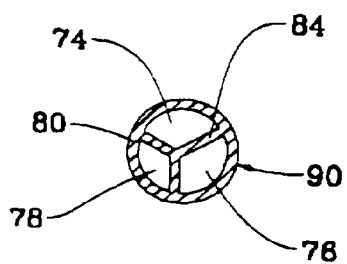


FIG. 14

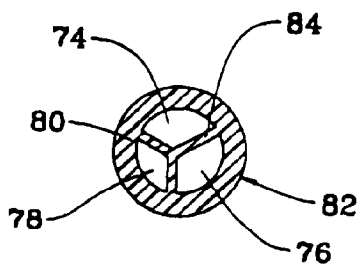


FIG. 15

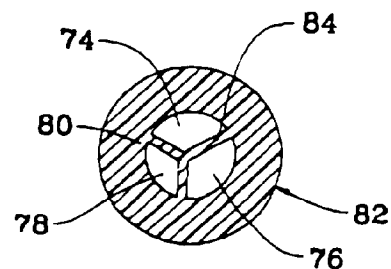


FIG. 17

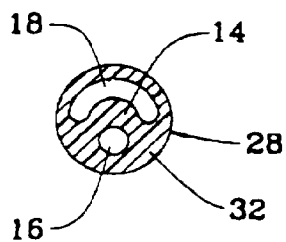


FIG. 18

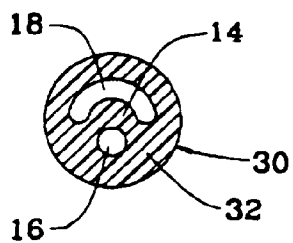


FIG. 19

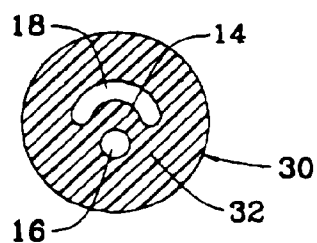
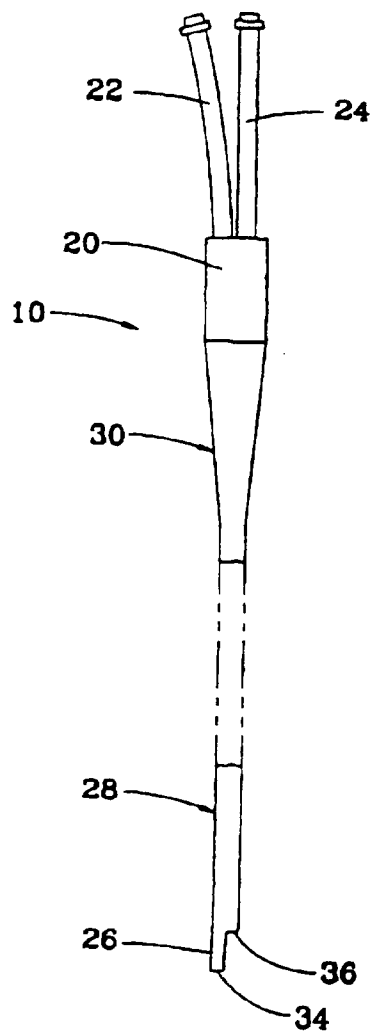


FIG. 20



INTERNATIONAL SEARCH REPORT

International application No.
PCT/US96/14972

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) : A61M 3/00, 25/00
US CL : 604/43, 280, 282, 364

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 128/772; 604/43, 104, 280, 282-284, 364; 606/108

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5,171,216 A (DASSE et al) 15 December 1992.	1-6, 8, 10, 12-15, 20, 21
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Y		7, 9, 11, 17-19, 22-27
X	US 4,769,005 A (GINSBURG et al) 06 September 1988.	1, 3, 5-9, 22, 23, 25, 26
X	US 4,236,520 A (ANDERSON) 02 December 1980.	1, 2, 6, 8
X	US 4,239,042 A (ASAI) 16 December 1980.	1, 3, 8

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

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Date of the actual completion of the international search
03 DECEMBER 1996

Date of mailing of the international search report
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(21) International Application Number: PCT/US99/01969 (22) International Filing Date: 28 January 1999 (28.01.99) (30) Priority Data: 60/073,213 30 January 1998 (30.01.98) US (71) Applicant (for all designated States except US): TYCO GROUP S.A.E.L. [US/US]; 6 avenue Emile Reuter, L-2420 Luxembourg (LU). (72) Inventor; and (75) Inventor/Applicant (for US only): GISSELBERG, Margo, L. [US/US]; 17229 33rd Place W., Lynwood, WA 98037 (US). (74) Agents: RACITI, Eric, P. et al.; Brown Rudnick Freed & Gesmer, P.C., One Financial Center, Boston, MA 02111 (US).		(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i> <i>With amended claims.</i>
(54) Title: MULTIPLE LUMEN CATHETER WITH AN ENLARGED TIP		
(57) Abstract <p>This invention is an elongate catheter (10) having one or more lumens (24, 26) therein, and at least one lumen in flow communication with an opening in the tip member (14) of the catheter. The tip member includes proximal area (15) for attachment of the tip member to the body portion (12) of the catheter, a flow passage area (17) having distal, proximal inner surfaces (32, 34) which taper outwardly from the interior of the catheter that includes a raised area (36) therebetween such that the openings are located on the same side of the catheter, and are spaced apart from each other with the raised area inbetween.</p>		

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MULTIPLE LUMEN CATHETER WITH AN ENLARGED TIP

Field of the Invention

The present invention relates generally to catheters for use on a human patient and more particularly to a multiple lumen catheter having an improved catheter tip. More particularly, the present invention includes a reinforced wall adjacent to a portion of the tip member and also preferably a lumen for the passage of a guide wire therethrough.

10 Background of the Invention

Single or multiple lumen catheters are well known in the medical field and are widely used in medical procedures such as hemodialysis or other procedures wherein it is desirable to inject or remove fluids through one or more lumens of the catheter. For example, in hemodialysis it is desirable to introduce blood into a vein or other vessel of a patient through a first lumen while simultaneously removing a corresponding amount of blood from the patient through a second lumen of the catheter. In certain situations, it may also be desirable to have a third lumen or fourth lumen extending through the catheter to allow a medication to be injected therethrough without interfering with the operation of the first or second lumens.

The currently available single or multiple lumen catheters frequently have an opening at the distal end thereof and one or more openings or holes along the sidewall of the catheter. During hemodialysis, the arterial or intake lumen is used to remove blood from the patient. This intake lumen typically opens along the sidewall of the catheter. In use, the side opening may occasionally become completely or partially occluded by the interior wall of the patient's blood vessel. The complete or partial occlusion of the side opening will significantly reduce the flow of blood through the intake lumen of the catheter and

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may also damage the interior wall of the patient's blood vessel.

In certain commercially available catheters, one or more relatively large side openings are used. With these
5 side openings it is typically recommended that the flow of fluid through the side opening be checked prior to hemodialysis. If the side opening is occluded, it is recommended that the catheter be rotated or otherwise repositioned. A further difficulty with the use of the
10 large single side opening is that the side opening may occasionally get caught on the tissue or the wall of the blood vessel during insertion into the patient. Yet another difficulty with the use of a large single side opening is that the catheter may kink or bend at the side opening
15 during insertion if the catheter tip meets resistance during insertion because the large side opening may weaken the column strength of the catheter.

In a commercially available catheter such as the catheter disclosed in U.S. Patent No. 4,543,087 granted to
20 Sommercorn et al., a plurality of spaced apart side openings are provided so that even if one side opening is occluded at least one of the remaining side openings may remain open. Another approach to solving the problem of occlusion is disclosed in U.S. Patent No. 4,795,439 granted
25 to Guest. In this patent, the lumens of the distal portion of the catheter are twisted such that the plurality of side openings in the catheter are not aligned in a straight line along the distal portion of the catheter.

The use of multiple side openings in a catheter
30 provides an increased likelihood that a clot may form along or in one or more of the side openings as compared to the likelihood of clotting in catheters with a single side opening for each lumen. This increased likelihood of clot formation is believed to be caused, at least partially, by
35 the presence of multiple surfaces between each of the side openings which may provide an area of reduced flow in the lumen which allows the clot to form thereon. Additionally,

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it is a common practice to prime the catheter lumens with heparin between treatments in order to decrease the likelihood of clot formation in the catheter. Priming the lumens with heparin is believed to be less effective in removing or preventing clot formation in catheters with multiple side openings because if one of the side openings is occluded by a clot, the heparin will merely flow through the side opening which provides the least resistance. There is also the possibility that the heparin may be washed out of the distal portion of the lumen of the catheter by blood which may enter one or more of the proximally located side openings to flush the heparin through the lumen and out of the catheter through one or more of the distally located side openings.

Several multiple lumen catheters are known in the art. For example, U.S. Patent No. 4,808,155 granted to Mahurkar is directed to a dual lumen catheter which is used primarily for hemodialysis. The catheter disclosed in this patent includes side by side lumens for the infusion and withdrawal of the patient's blood. As shown, the withdrawal lumen is substantially shorter than the infusion lumen to minimize the mixing of the treated and untreated blood of the patient.

In U.S. Patent No. 5,571,093 granted to Cruz et. al. A multiple lumen catheter is shown which includes a pair of side by side lumens having the distal openings to the lumens spaced apart from each other and opening on the same side of the catheter tip. One potential disadvantage of this type of catheter is that the tip of the catheter may fold over on itself during use. Additionally, a common approach to catheter placement is the Seldinger technique which requires the use of a guide wire during placement of the catheter. The design disclosed in the Cruz patent is not readily adaptable for use with this technique.

Accordingly, there is a need for a catheter capable of overcoming the problems described above as well as others,

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such as catheter whipping and the mixing of fluids from the two lumens at the tip portion of the catheter.

Summary of the Present Invention

5 The present invention is intended to provide an improved tip for a catheter. The catheter tip preferably minimizes whipping or bending of the catheter tip while reducing the mixing of fluids from the catheter. Additionally, the present invention enables the physician to insert the catheter using conventional placement
10 techniques while reducing the likelihood of positional occlusion of the catheter.

According to a preferred form of the present invention, the catheter includes a pair of side by side lumens which extend from the proximal end portion of the
15 tubing to the distal end portion of the tubing. The tip portion is preferably attached to the distal end portion of the tubing and includes distal and proximal end portions thereon. The preferred form of the catheter is a dual lumen catheter having at least one generally D shaped lumen
20 therein. The catheter preferably includes a blood return or first lumen which extends between the proximal end portion of the catheter and the distal end portion of the catheter tip. The other lumen is preferably an intake or second lumen which extends between the proximal end portion of the
25 catheter and a side opening generally at the interconnection of the distal end portion of the catheter and the proximal end portion of the catheter tip. The tip portion preferably includes distal and proximal end portions wherein the connection portion is located along
30 the proximal end portion of the tip and the distal end portion is generally bulbous shaped with a relatively small guide wire passing lumen extending therethrough. The sidewall of the tubing portion of the distal end portion of the catheter preferably extends beyond the opening of the
35 second lumen on the side of the catheter which is opposite opening to reinforce the catheter to minimize buckling.

- 5 -

Another object of the present invention is to prevent clotting by providing a side opening in the sidewall of a catheter which is shaped and oriented to be essentially self flushing such that external fluid flow may pass
5 directly from the proximal side of the side opening to the distal side of the side opening without interruption.

Yet another object of the present invention is to reduce vessel wall occlusion by providing a side opening which maximizes the open passageway for fluid flow even
10 when a portion of the slot is occluded by or sucked against a portion of the vessel wall.

Brief Description of the Drawings

Figure 1 is an elevated view of a catheter of the present invention;

15 Figure 2 is an enlarged elevated view of the distal portion of the embodiment shown in Figure 1;

Figure 3 is an enlarged side view of the distal portion of the embodiment shown in Figure 1;

20 Figure 4 is an enlarged cross-sectional view of the distal portion of the embodiment shown in Figure 1, taken generally along lines 4-4 of Figure 2;

Figure 5 is a cross-sectional view of the embodiment shown in Figure 1 taken generally along lines 5-5 of Figure 2;

25 Figure 6 is a cross-sectional view of the embodiment shown in Figure 1 taken generally along lines 6-6 of Figure 2; and

Figure 7 is an end view of the catheter of Figure 1.

Description of the Preferred Embodiments

30 The preferred form of the overall catheter assembly 10 of the present invention is generally shown in the drawings. The catheter assembly 10 generally includes an elongate and slightly oval-shaped body portion 12 having a tip member 14 on the distal end thereof and a Y-shaped
35 connector hub 16 on the proximal end thereof. As shown in

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Figure 1, the proximal end of the Y-connector includes extension members 18 and 20 thereon. The extension members 18 and 20 may be bent as shown or straight (not shown). As used herein, the term "proximal" is intended to refer to the end or portion of a member which is normally oriented or positioned away from the patient while the term "distal" refers to the end or portion of a member in use which is nearest to the patient. Although the preferred form of the present invention is described herein with respect to multiple lumen catheters, it is intended that the present invention may also be used with nearly any catheter having one or more lumens therein including angiographic, central venous, hemodialysis or various other catheters.

The body portion 12 of the preferred embodiment of the catheter assembly 10 is hollow except for a generally flat, longitudinal septum 22 which divides the interior of the hollow cylinder into two preferably parallel lumens 24 and 26, with each lumen, 24 and 26, having a generally D-shaped cross section. As illustrated by the arrows in Figure 4, the lumen 24 is the blood intake or arterial lumen, and the lumen 26 is the blood return or venous lumen when this invention is used for a procedure such as hemodialysis.

At the distal end of the catheter assembly 10, the exterior surface of the body portion 12 preferably merges smoothly into the tip member 14. The body of the tip member 14 is preferably formed by injection molding and may be adhesively, heat or otherwise attached or bonded to the distal end portion of the body portion in a conventional manner. Additionally, the tip may also be insert molded directly onto the distal end portion of the body portion. The tip member preferably includes three areas. The proximal area 15 is the connection area where the tip member 14 and body portion 12 are interconnected. As shown in the drawings, the proximal area 15 is generally staggered so that the outer wall of the body portion 12 which is oriented adjacent to the side of the intake lumen 24 is proximal to the portion of the body portion 12 which

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forms the septum 22 and the outer wall of the body portion 12 which is adjacent to the return lumen 26 extends beyond the septum 22 and outer wall of the body portion which is adjacent to the intake lumen. As shown in the drawings, the proximal side of the proximal area 15 generally forms the opening 30 for the intake lumen 24.

The middle portion of the tip member 14 is generally referred to as the flow passage area 17. The flow passage area 17 preferably includes a pair of flow directing inner surfaces. The proximal inner surface 32 directs the flow of fluid from the blood vessel of the patient into the catheter when the catheter is used for hemodialysis and has sufficient surface area and tapered surfaces to minimize the likelihood that the opening 30 for the intake lumen 24 will not be caught against the wall of the blood vessel. Additionally, the proximal inner surface 32 is shaped to disperse any fluids which are injected into the blood vessel of the patient through this lumen when the flow of fluids is reversed. The distal inner surface 34 of the flow passage area 17 is adjacent to the opening 28 for the return lumen 26 to disperse and direct the fluids passing from the opening 28 into the blood vessel of the patient when the catheter is used for hemodialysis or the injection of fluids or medications into the patient. As with the proximal inner surface 32, the distal inner surface 34 is shaped to minimize the likelihood that the opening 28 will be drawn against the wall of the blood vessel if fluids are drawn into the catheter through the opening 28 because of the shape of the distal inner surface 34. Additionally, the existence of the guide wire lumen 38 in fluid communication with the return lumen 26 will prevent the opening 28 from being drawn up against the wall of the blood vessel because fluid will continue to flow through the distal most opening 40 which is preferably located on the distal end of the tip member 14. As shown, the flow passage area 17 also includes a raised area 36 which functions to reduce the likelihood that fluids will be intermixed between the openings 28 and

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30 because fluids injected through the opening 30 will contact and be dispersed by the proximal inner surface 32 and the raised area 36.

5 The final area of the tip member 14 is the nose area 19. This area is an enlarged area located on the distal end portion of the tip member 14. The nose area 19 is a generally bullet shaped area which functions to disperse fluids from the return lumen and also includes the guide wire lumen 38 extending therethrough.

10 The outer diameter of the tip member 14 decreases from the proximal area 15 of the nose area 19. At the proximal portion of the nose area 19, the diameter of the tip member is approximately equal to or slightly less than the diameter of the body portion 12 of the catheter assembly
15 10. As shown in Figure 4, the interconnection of the tip member 14 and the body portion rely on the engagement of the walls of the body portion and the tip member which as mentioned above, may be adhesively or otherwise bonded together in a conventional manner. The wall of the body
20 portion 12 which is opposite to the opening 30 extends into the tip member 14 and preferably forms a surface for binding the components together as well as a surface which adds longitudinal strength to the tip member 14. In the preferred form of this invention, the tip member 14 is
25 formed of a relatively soft material so as to minimize the potential for injury to the wall of the blood vessel while the body portion is preferably stiffer than the tip member 14 to provide greater columnar strength to the catheter assembly to allow for the insertion of the catheter into
30 the body of the patient.

As shown in Figures 2 and 3, the openings 28 and 30 of the lumens of the catheter preferably extend the entire width of the tip member 14 and are separated longitudinally along the tip member 14 by the raised area 36.
35 Additionally, the relative area of the openings 28 and 30 at the proximal inner surface 32 and distal inner surface 34 is preferably greater than the area of the lumens 24 and

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26 along the length of the body portion 12. The proximal and distal inner surfaces, 32 and 34, preferably curve radially away from the axis of the tip member 14. The shape of the proximal and distal inner surfaces 32 and 34, 5 generally determines the shape of the openings 30 and 28 respectively. These openings are preferably formed to extend more than 180 degrees around the circumference of the tip member 14. Therefore, fluids delivered outwardly through the lumens 24 and 26 pass around and over a large 10 portion of surface area of the raised area 36 and nose area 19. Therefore, the tendency for the tip member to whip in the blood vessel during use is reduced. The proximally positioned portion of the raised area 36 and nose area 19 adjacent to the openings 28 and 30 are each gradually built 15 up in the distal direction to define a preferably uniform arc terminating along the outer surface of the tip member 14. In the preferred form of this invention, the radius of this arc is relatively short and is preferably as large as the intake and return lumens, 24 and 26 respectively. 20 Additionally, the taper on the proximal side of each of the openings 28 and 30 is much sharper than the gradually tapered surfaces on the distal side of the openings formed by the proximal and distal inner surfaces, 32 and 34.

While the foregoing description has been drawn to the 25 presently preferred embodiment of the present invention, it should be understood by those skilled in the art of the present subject matter that various modifications may be made to the present invention without departing from the scope and spirit of the invention which is defined by the 30 following claims.

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MULTIPLE LUMEN CATHETER WITH AN ENLARGED TIP

Claims

1. An elongate catheter comprising:
an elongate body portion formed by a circumferential sidewall with a septum extending therebetween and having a longitudinal axis and distal and proximal end portions thereon;
5 a first lumen in said body portion extending between said proximal end portion and said distal end portion;
a second lumen in said body portion extending between said proximal end portion and said distal end portion;
10 a tip member extending from said distal end portion of said body portion;
said tip member including a proximal area connected to said distal end portion of said body portion and a flow passage area distally of said proximal area;
15 said tip member further including a nose area on said tip member wherein said nose area is located distally of said flow passage area and includes a lumen extending therethrough; and
20 a plurality of openings on said tip member which are interconnected with said first and second lumens and said plurality of openings are spaced apart from each other by a raised area on said flow passage area of said tip member.
2. The catheter of claim 1 wherein said body portion includes said first and second lumens therein formed by said septum and said circumferential sidewall and extending longitudinally along said body portion, and said second lumen extends between said proximal end portion and a location between said distal end portion of said body portion and said raised area on said flow passage area of said tip member.
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3. The catheter of claim 1 wherein said second lumen extends between said proximal end portion and a location distally of said raised area on said flow passage area of said tip member.

4. The catheter of claim 3 wherein said second lumen is in flow communication with at least one of said plurality of openings and said lumen in said nose area on said tip member and wherein said at least one of said
5 plurality of openings opens on said tip member between said raised area of said flow passage area and between said nose area of said tip member.

5. The catheter of claim 1 wherein the interconnection of said tip member and said body portion is staggered such that the portion of said sidewall which is adjacent to first lumen is shorter than the portion of said
5 sidewall which is adjacent to said second lumen.

6. The catheter of claim 1 wherein said body portion is interconnected with said tip member and the interconnection of said tip member and said body portion is staggered such that the interconnection between said septum
5 and said tip member is intermediate to the interconnection of a portion of said sidewall adjacent to said first and second lumens and wherein the interconnection of said first lumen with said tip member is proximal of the interconnection of said second lumen and said tip member.

7. The catheter of claim 1 wherein said body portion is interconnected with said tip member and said septum is interconnected with said raised area of said flow passage area of said tip member and a portion of said sidewall
5 adjacent to said second lumen is interconnected to said tip member at a location distally of said interconnection of said septum and said tip member.

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8. The catheter of claim 1 wherein said lumen of said nose area extends to the distal end of said tip member to form an opening thereon.

9. The catheter of claim 1 wherein the circumference of body portion is greater than the circumference of said tip member adjacent to at least a portion of said flow passage area.

10. The catheter of claim 1 wherein said tip member includes a proximal inner surface adjacent to said first lumen and said proximal inner surface tapers outwardly from said septum to form said raised area in said flow passage area of said tip member.

11. The catheter of claim 10 wherein said proximal inner surface forms an arcuate raised area on said flow passage area of said tip member.

12. The catheter of claim 1 wherein said tip member includes a distal inner surface adjacent to said second lumen and said distal inner surface tapers inwardly from said nose area to a location adjacent to said raised area of said tip member.

13. The catheter of claim 12 wherein said distal inner surface forms an arcuate raised area on said flow passage area of said tip member.

14. An elongate catheter comprising:
an elongate body portion formed by a circumferential sidewall with a septum extending therebetween and having a longitudinal axis and distal and proximal end portions thereon;
a first lumen in said body portion formed between at least a portion of said circumferential sidewall and

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said septum and extending between said proximal end portion and said distal end portion of said body portion;

10 a second lumen in said body portion formed between at least a portion of said circumferential sidewall and said septum and extending between said proximal end portion and said distal end portion of said body portion;

15 a tip member extending from said distal end portion of said body portion;

 said tip member including a proximal area connected to said distal end portion of said body portion and a flow passage area distally of said proximal area;

20 said tip member further including a nose area on said tip member wherein said nose area is located distally of said flow passage area and includes a lumen extending therethrough; and

 a first opening on said tip member in flow communication with said first lumen and a second opening on said tip member in flow communication with said second lumen and said lumen in said nose area forming a third opening on said tip member and wherein said first and second openings are spaced apart from each other on said tip member by a raised area of said flow passage area
30 wherein said raised area is formed by at least part of a proximal inner surface which tapers outwardly from said septum.

15. The catheter of claim 14 wherein the interconnection of said tip member and said body portion is staggered such that the portion of said sidewall which is adjacent to first lumen is shorter than the portion of said
5 sidewall which is adjacent to said second lumen.

16. The catheter of claim 14 wherein said body portion is interconnected with said tip member and the interconnection of said tip member and said body portion is staggered such that the interconnection between said septum
5 and said tip member is intermediate to the interconnection

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of a portion of said sidewall adjacent to said first and second lumens and wherein the interconnection of said first lumen with said tip member is proximal of the interconnection of said second lumen and said tip member.

17. The catheter of claim 14 wherein said body portion is interconnected with said tip member and said septum is interconnected with said raised area of said flow passage area of said tip member and a portion of said
5 sidewall adjacent to said second lumen is interconnected to said tip member at a location distally of said interconnection of said septum and said tip member.

18. The catheter of claim 14 wherein the circumference of body portion is greater than the circumference of said tip member adjacent to at least a portion of said flow passage area.

19. The catheter of claim 14 wherein said tip member include said proximal inner surface adjacent to said first lumen and said proximal inner surface tapers outwardly from said septum to form said raised area in said flow passage
5 area of said tip member and said proximal inner surface forms an arcuate raised area on said flow passage area of said tip member.

20. The catheter of claim 14 wherein said tip member includes a distal inner surface adjacent to said second lumen and said distal inner surface tapers inwardly from said nose area to a location adjacent to said raised area
5 of said tip member.

21. The catheter of claim 20 wherein said distal inner surface forms an arcuate raised area on said flow passage area of said tip member.

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22. The catheter of claim 14 wherein said first and second openings are spaced apart from each other and are located on the same side of the catheter.

AMENDED CLAIMS

[received by the International Bureau on 14 June 1999 (14.06.99);
original claims 1 and 14 amended; new claim 23 added;
remaining claims unchanged (4 pages)]

1. An elongate catheter comprising:

an elongate body portion formed by a circumferential sidewall with a septum extending therebetween and having a longitudinal axis and distal and proximal end portions thereon;

a first lumen in said body portion extending between said proximal end portion and said distal end portion;

a second lumen in said body portion extending between said proximal end portion and said distal end portion;

a tip member extending from said distal end portion of said body portion;

said tip member including a proximal area connected to said distal end portion of said body portion and a flow passage area distally of said proximal area;

said tip member further including a nose area on said tip member wherein said nose area is located distally of said flow passage area and includes a lumen extending therethrough; and

a plurality of openings on said tip member which are interconnected with said first and second lumens and said plurality of openings are spaced apart from each other by a raised area on said flow passage area of said tip member.

2. The catheter of claim 1 wherein said body portion includes said first and second lumens therein formed by said septum and said circumferential sidewall and extending longitudinally along said body portion, and said second lumen extends between said proximal end portion and a location between said distal end portion of said body portion and said raised area on said flow passage area of said tip member.

8. The catheter of claim 1 wherein said lumen of said nose area extends to the distal end of said tip member to form an opening thereon.

9. The catheter of claim 1 wherein the circumference of body portion is greater than the circumference of said tip member adjacent to at least a portion of said flow passage area.

10. The catheter of claim 1 wherein said tip member includes a proximal inner surface adjacent to said first lumen and said proximal inner surface tapers outwardly from said septum to form said raised area in said flow passage area of said tip member.

11. The catheter of claim 10 wherein said proximal inner surface forms an arcuate raised area on said flow passage area of said tip member.

12. The catheter of claim 1 wherein said tip member includes a distal inner surface adjacent to said second lumen and said distal inner surface tapers inwardly from said nose area to a location adjacent to said raised area of said tip member.

13. The catheter of claim 12 wherein said distal inner surface forms an arcuate raised area on said flow passage area of said tip member.

14. An elongate catheter comprising:

an elongate body portion formed by a circumferential sidewall with a septum extending therebetween and having a longitudinal axis and distal and proximal end portions thereon;

a first lumen in said body portion formed between at least a portion of said circumferential sidewall and

said septum and extending between said proximal end portion and said distal end portion of said body portion;

a second lumen in said body portion formed between at least a portion of said circumferential sidewall and said septum and extending between said proximal end portion and said distal end portion of said body portion;

a tip member extending from said distal end portion of said body portion;

said tip member including a proximal area connected to said distal end portion of said body portion and a flow passage area distally of said proximal area;

said tip member further including a nose area on said tip member wherein said nose area is located distally of said flow passage area and includes a lumen extending therethrough; and

a first opening on said tip member in flow communication with said first lumen and a second opening on said tip member in flow communication with said second lumen and said second lumen in said nose area forming a third opening on said tip member and, wherein said first and second openings are spaced apart from each other on said tip member by a raised area of said flow passage area wherein said raised area is formed by at least part of a proximal inner surface which tapers outwardly from said septum.

15. The catheter of claim 14 wherein the interconnection of said tip member and said body portion is staggered such that the portion of said sidewall which is adjacent to first lumen is shorter than the portion of said sidewall which is adjacent to said second lumen.

16. The catheter of claim 14 wherein said body portion is interconnected with said tip member and the interconnection of said tip member and said body portion is staggered such that the interconnection between said septum and said tip member is intermediate to the interconnection

22. The catheter of claim 14 wherein said first and second openings are spaced apart from each other and are located on the same side of the catheter.

23. An elongate catheter comprising:

an elongate body portion formed by a circumferential sidewall with a septum extending therebetween and having a longitudinal axis and distal and proximal end portions thereon;

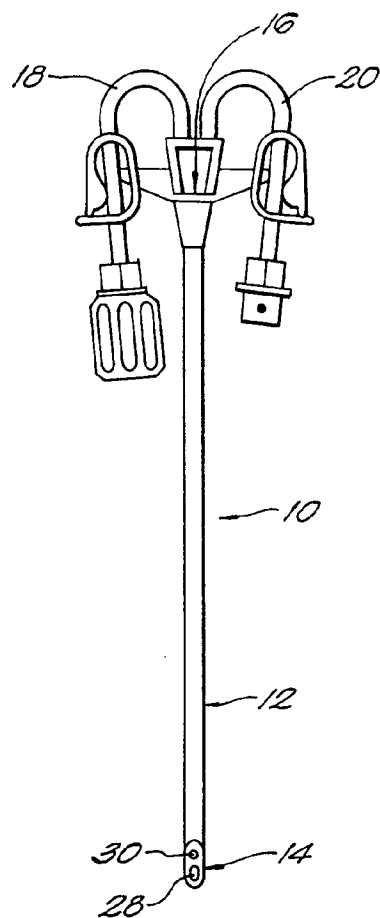
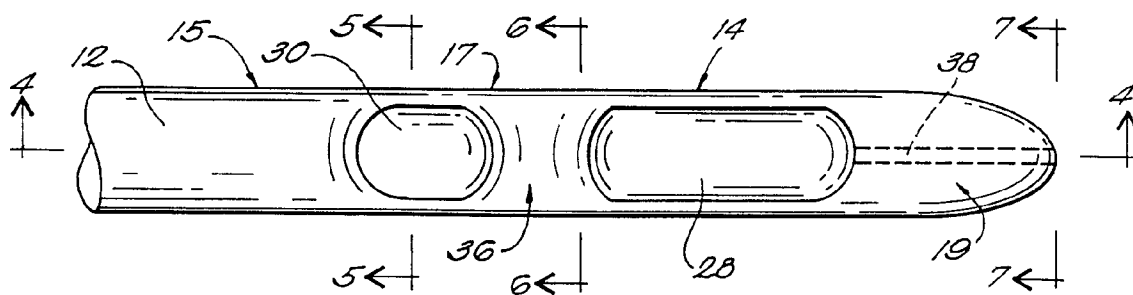
a first lumen in said body portion formed between at least a portion of said circumferential sidewall and said septum and extending between said proximal end portion and said distal end portion of said body portion;

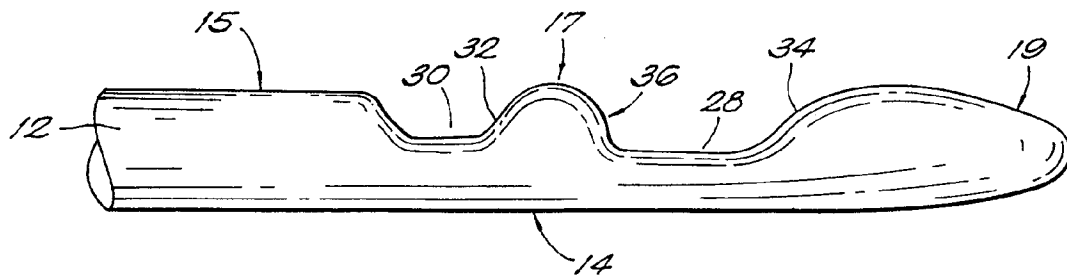
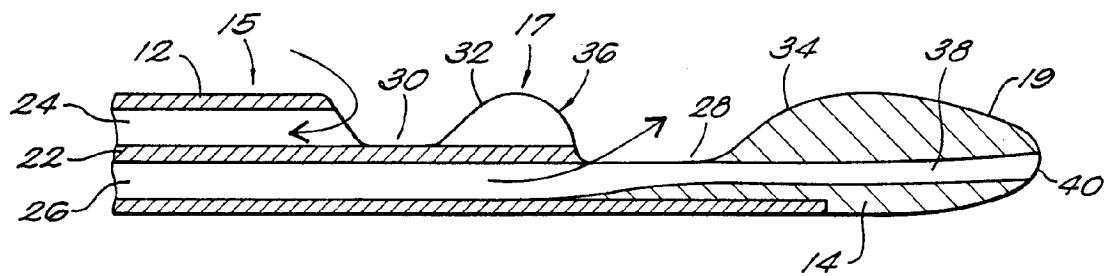
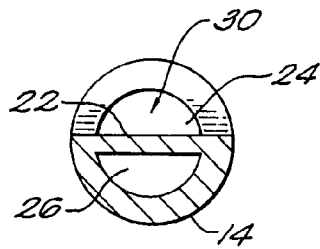
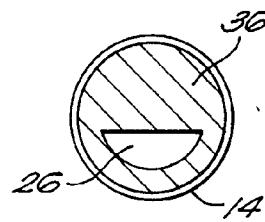
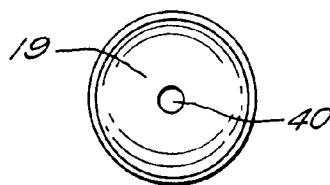
a second lumen in said body portion formed between at least a portion of said circumferential sidewall and said septum and extending between said proximal end portion and said distal end portion of said body portion;

a tip member extending from said distal end portion of said body portion and including a proximal area connected to said distal end portion and a flow passage area distally of said proximal area;

said tip member further including a nose area having a distal nose end portion wherein said nose area is located distally of said flow passage area and includes a lumen extending therethrough to said distal nose end portion; and

a first opening on said tip member in flow communication with said first lumen and a second opening on said tip member in flow communication with said second lumen and said second lumen in said nose area forming a third opening at said distal nose end portion and, wherein said first and second openings are spaced apart from each other on said tip member by a raised area of said flow passage area wherein said raised area is formed by at least part of a proximal inner surface which tapers outwardly from said septum.

**FIG. 1****FIG. 2**
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**FIG. 3****FIG. 4****FIG. 5****FIG. 6****FIG. 7**
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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/01969

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) : A61M 3/00

US CL : 604/35, 43

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 604/35, 39, 43, 264, 268, 284, 538

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

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C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 4,995,865 A (GAHARA et al.) 26 February 1991, Fig. 2.	1, 14
A	US 5,472,417 A (MARTIN et al.) 05 December 1995, Fig. 3.	1, 14
A	US 5,380,276 A (MILLER et al.) 10 January 1995, Fig. 2.	1, 14
A	US 5,685,867 A (TWARDOWSKI et al.) 11 November 1997, Figs. 3-12.	1, 14
X	US 5,571,093 A (CRUZ et al.) 05 November 1996, Figs. 11-15.	1-14
Y	US 5,451,206 A (YOUNG) 19 September 1995, Figs. 12-14 for the third opening.	14

☐ Further documents are listed in the continuation of Box C.☐ See patent family annex.

* Special categories of cited documents:	*T	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
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Date of the actual completion of the international search

24 MARCH 1999

Date of mailing of the international search report

15 APR 1999

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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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(21) International Application Number: PCT/US00/05154 (22) International Filing Date: 29 February 2000 (29.02.00) (30) Priority Data: 60/123,474 9 March 1999 (09.03.99) US 09/282,921 31 March 1999 (31.03.99) US (71) Applicant: DURECT CORPORATION [US/US]; 10240 Bubb Road, Cupertino, CA 95014 (US). (72) Inventors: GILLIS, Edward, M.; 1202 Stafford Drive, Cupertino, CA 95014 (US). THEEUWES, Felix; 27350 Altamont Road, Los Altos Hills, CA 94022 (US). (74) Agent: FRANCIS, Carol, L.; Bozicevic, Field & Francis LLP, Suite 200, 200 Middlefield Road, Menlo Park, CA 94025 (US).		(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>Without international search report and to be republished upon receipt of that report.</i>
(54) Title: IMPLANTABLE DEVICE FOR ACCESS TO A TREATMENT SITE <div data-bbox="305 1157 1265 1430" data-label="Image"> </div> (57) Abstract <p>The present invention provides an implantable guide for access to a treatment site. The implantable guide comprises a proximal end, a distal end, and a guide body defining a lumen, and can optionally comprise a stable positioning element for stably positioning a drug delivery device within the guide. The guide can be provided in connection with a drug delivery device. In use, the guide is implanted within a subject so as to provide a conduit through which a drug delivery device can be retrievably introduced to facilitate delivery of drug to a treatment site within a subject at a site distal to an accessible implantation site. The drug delivery device is then positioned within the guide lumen to provide for delivery of drug from the drug delivery to the desired treatment site.</p>		

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IMPLANTABLE DEVICE FOR ACCESS TO A TREATMENT SITE

FIELD OF THE INVENTION

This invention relates generally to implantable devices and methods of use relating to
5 same, particularly to site-specific drug delivery.

BACKGROUND OF THE INVENTION

Few therapeutic regimen involve administration of a single dose of a selected drug.
Instead, most therapies require administration of multiple doses. Where the therapy requires
10 parenteral delivery of the drug, the patient can be subjected to the substantial discomfort and
inconvenience of repeated injections. This can be particularly problematic where the condition or
disease to be treated requires long-term therapy. The repeated injections required for such long-
term therapy not only meet with difficulties associated with patient compliance, but also can lead
to collapse of veins and substantial tissue damage. Parenteral drug delivery typically also requires
15 administration of a bolus of drug in order to provide for an effective drug concentration at the
desired treatment site and/or to provide for an adequate systemic levels for an acceptable period of
time (*e.g.*, as in treatment of diabetes with insulin). Delivery of a drug bolus not only requires
delivery of a greater amount of drug, thus driving up the cost of therapy, but can also be associated
with undesirable side effects.

20 One approach for avoiding at least some of the problems inherent in long-term drug
delivery involves the use of an implantable drug delivery device. Examples of such implantable
drug delivery devices include implantable diffusion systems (see, *e.g.*, subdermal implants (such
as NORPLANT™) and other such systems, see, *e.g.*, U.S. Pat. Nos. 5,756,115; 5,429,634;
5,843,069). These implants generally operate by simple diffusion, *e.g.*, the active agent diffuses
25 through a polymeric material at a rate that is controlled by the characteristics of the active agent
formulation and the polymeric material. An alternative approach involves the use of biodegradable
implants, which facilitate drug delivery through degradation of the implant material that contains
the drug (see, *e.g.*, U.S. Pat. No. 5,626,862). Alternatively, the implant may be based upon an
osmotically-driven device to accomplish controlled drug delivery (see, *e.g.*, U.S. Pat. Nos.
30 3,987,790, 4,865,845, 5,057,318, 5,059,423, 5,112,614, 5,137,727, 5,234,692; 5,234,693; and
5,728,396). These osmotic pumps generally operate by imbibing fluid from the outside
environment and releasing corresponding amounts of the therapeutic agent.

While such drug delivery devices avoid the need for repeated injection often associated with long-term drug therapies, the treatment site to which drug delivery is desired is often not amenable to insertion of such an implant. For example, while such implants may be useful in delivering a chemotherapeutic to a localized breast tumor, there are many sites within the body (e.g., a site deep within a subject's body) or to a site that is particularly fragile or sensitive (e.g., the spinal cord) where the implant cannot be easily or practically inserted. Although these implants could instead be used to deliver the drug systemically, systemic delivery is often not an acceptable form of long-term drug delivery. Many therapeutic drugs are highly toxic and/or may cause dangerous side effects. Moreover, systemic administration normally requires administration of higher doses in order to provide an effective concentration at a desired treatment site, making therapies more likely to be associated with side-effects and more expensive.

Implantable infusion devices having an associated drug delivery catheter avoid at least some of the problems associated with the implantable diffusion systems and biodegradable systems described above. Implantable infusion devices can control delivery of drug by, for example, use of a programmable pump that controls release of the drug from a reservoir at a certain rate to a desired treatment site (see, e.g., U.S. Pat. Nos. 4,692,147; 5,713,847; 5,711,326; 5,458,631; 4,360,019; 4,487,603; and 4,715,852). Alternatively, implantable infusion devices can control drug delivery by means of a rate-limiting membrane positioned between the drug reservoir and the delivery catheter (see, e.g., U.S. Pat. No. 5,836,935), or by only releasing drug from the reservoir upon application of pressure to a subcutaneously positioned device (see, e.g., U.S. Pat. No. 4,816,016; 4,405,305). Implantable infusion devices have been described for intravenous, intra-arterial, intrathecal, intraperitoneal, intraspinal and epidural drug delivery. In general, these pumps are usually surgically inserted into a subcutaneous pocket of tissue (e.g., in the lower abdomen), and a catheter attached to the pump is positioned at a desired treatment site (see, e.g., 4,692,147).

While implantable infusion devices with associated drug delivery catheters can facilitate delivery of drug at a higher concentration to a desired treatment site, these devices also meet with limitations. First, the drug delivery catheter may be difficult to position to gain access to the area of the body where drug delivery is desired, e.g., the drug delivery catheter may be limited in its length, or relatively inflexible or otherwise difficult to shape to the tortuous bends in the drug delivery pathway to the treatment site. Second, if the drug delivery catheter is removed or disturbed in order to replenish or replace the drug contained in the infusion device, the entire, tedious procedure for positioning the drug delivery catheter must be repeated.

One method of avoiding constant repositioning of the drug delivery catheter is by having a self-sealable septum associated with the drug reservoir of the infusion device and positioned outside or just under the skin to allow for injection of additional drug into the reservoir (see, *e.g.*, U.S. Patent Nos. 5,713,858; 5,836,935; 4,816,016; 4,405,305; 5,092,849; 4,929,236; and 5,085,656). However, this method requires the patient be subjected to frequent injections. Furthermore, drug delivery is generally limited to only the region surrounding locations within the body where the infusion device may be implanted, *i.e.*, the device must be implanted so as to allow easy access for injections. Another method of avoiding constant catheter repositioning uses a drug delivery catheter that can be disengaged from the drug delivery device (see, *e.g.*, U.S. Pat. Nos. 5,713,847; 4,692,147; 5,711,316). However, such detachment and reattachment of the drug delivery catheter from the drug delivery device increases the risk of leakage, as well as the risk of contaminants being introduced into the drug delivery pathway.

Still another method for avoiding the repositioning the drug delivery catheter involves a device that is inserted into the subject to maintain a conduit from an external access site to the desired treatment site (see, *e.g.*, U.S. Pat. Nos. 5,792,110; 5,542,923; 5,702,363; 5,053,013; 4,769,005; 5,004, 457; 5,135,525; 4,966,588; 5,257,980; 5,522,803; 4,578,061; 5,464,395; and 4,755,173). However, presently available methods and devices for maintaining such conduits are not completely implantable within the subject, are not suitable for long-term drug delivery, and/or do not provide for delivery of drug to a site deep within the body (*e.g.*, a treatment site other than a subcutaneous or subdermal treatment site). For example, use of such devices is often associated with substantial discomfort or inconvenience to the subject (*e.g.*, due to the use of, for example, a rigid, trocar-like device to maintain the conduit to the treatment site, see, *e.g.*, U.S. Pat. No. 5,792,110), or require the use of equipment that makes such devices and methods impractical for long-term therapy (see, *e.g.*, U.S. Pat. No. 5,004,457). Other presently available devices and methods require the use of a needle, which can cause substantial discomfort to the patient, is generally not suitable for long-term implantation, and thus is generally not suitable for long-term therapy (see, *e.g.*, U.S. Pat. Nos. 5,257,908; 5,522,803; 4,578,061; 5,464,395; 5,464,395; and 4,755,173).

There is a need in the field for a drug delivery system that is completely implantable and provides for convenient, repeated access to a treatment site. The present invention addresses these problems.

SUMMARY OF THE INVENTION

The present invention provides an implantable guide for access to a treatment site. The implantable guide comprises a proximal end, a distal end, and a guide body defining a lumen, and can optionally comprise a stable positioning element for stably positioning a drug delivery device within the guide. The guide can be provided in connection with a drug delivery device. In use, the guide is implanted within a subject so as to provide a conduit through which a drug delivery device can be retrievably introduced to facilitate delivery of drug to a treatment site within a subject at a site distal to an accessible implantation site. The drug delivery device is then positioned within the guide lumen to provide for delivery of drug from the drug delivery to the desired treatment site.

10 In one aspect the invention features an implantable guide for facilitating repeated access to a treatment site in a subject, where the guide comprises a proximal end, a distal end, a guide body, and a stable positioning element. The guide body defines a lumen extending from the guide proximal end to the guide distal end, and the stable positioning element facilitates stable positioning at least a portion of a drug delivery device within the guide for delivery of a drug from the drug delivery device and through the guide distal end.

15 In another aspect, the invention features a system for delivery of drug to a treatment site comprising 1) a flexible guide comprising a proximal end, a distal end, a guide body, and a stable positioning element, where the guide body defines a lumen extending from the guide proximal end to the guide distal end; and 2) a drug delivery device at least a portion of which is removably and stably positioned within the guide lumen. The drug delivery device is positioned for delivery of drug from a drug reservoir of the drug delivery device and through the distal end of the guide lumen. In specific embodiments, the drug delivery device comprises a drug release device comprising a drug reservoir, a distal portion defining a drug delivery orifice, and a drug delivery catheter comprising a drug delivery catheter proximal end and a drug delivery catheter distal end, 20 where the drug delivery catheter proximal end is coupled to the drug release device to provide a drug delivery pathway from the drug reservoir, through the orifice, and through a lumen of the drug delivery catheter to the drug delivery catheter distal end. The drug release device is positioned at the guide proximal end and the drug delivery catheter is positioned within the guide lumen.

30 In still another aspect the invention features a drug delivery device adapted for retention in a guide of the invention. The drug delivery device comprises a drug release device and a drug delivery catheter. The drug release device distal portion defines an orifice. The drug delivery catheter comprises a proximal end and a distal end, with the proximal end being coupled to the

drug release device to provide a drug flow pathway from the reservoir, through the orifice, and through a lumen of the drug delivery catheter.

In another aspect the invention features a method for site-specific drug delivery. The method comprises the steps of implanting a guide into a subject to provide for placement of the guide catheter distal end at a treatment site, and inserting a drug delivery device into the implanted
5 guide so that the drug delivery device is stably positioned at a proximal end of the guide and provides for delivery of drug to a distal end of the guide and to the treatment site.

In another aspect the invention features a method of providing access to a treatment site by implanting a guide of the invention into a subject to provide for placement of the guide distal end at
10 a treatment site, thereby defining a conduit for access to the treatment site.

A primary object of the invention is to provide for a drug delivery system that is completely implantable and allows convenient placement of a drug delivery device and replacement of the drug delivery device without loss of access to the treatment site.

It is another object of the invention to provide a drug delivery system that can be used with
15 a variety of drug release devices to accomplish site-specific drug delivery.

An important advantage of the invention is that the invention facilitates access and re-access of a drug delivery system to the site where drug is desired to be delivered.

Another important advantage of the invention is that the clinician or other user avoids the tedium of re-accessing the treatment site after removal of the drug delivery device and drug
20 delivery catheter.

Another advantage of the invention is that the need for a fluid path coupler, such as that required in detachable drug infusion pump and catheter system, is completely avoided. For example, replacement of the drug delivery device does not require detaching the portion of the drug delivery device housing the drug reservoir from the drug delivery catheter, thus risking
25 contamination of the drug delivery catheter and thus delivery of such contaminants to the treatment site.

Another advantage of the invention is that the drug delivery device can be removed and replaced without coupling and uncoupling the actual drug conduit from the drug release device, thus substantially reducing risk of leakage of drug from the drug release device.

Another advantage is that the drug delivery device can be supplied so that it is primed with drug, *e.g.*, the drug delivery catheter of the device is substantially filled with drug, thus reducing
30 delivery start-up time, *i.e.*, time related to movement of the drug from the drug release device to

the distal end of the drug delivery catheter. This feature is particularly advantageous where the drug release device releases drug at relatively low flow rates (*e.g.*, 0.4 μ l/day).

Still another advantage of the invention is that the invention can use a material that is relatively more difficult to implant (*e.g.*, a relatively stiff catheter material) for the drug delivery catheter in combination with a guide comprising a material that is relatively easier to implant. Thus, the guide can be designed to facilitate placement of the drug delivery catheter at the treatment site with minimal trauma to the subject, *e.g.*, once in place, the guide protects the subject during placement of the stiffer drug delivery catheter to provide for delivery of drug to the treatment site.

Another advantage of the invention is that the invention can be used in a variety of therapeutic and diagnostic applications. For example, the invention can be used to accomplish controlled delivery of a relatively small amount of drug over a selected period of time (*e.g.*, several hours to several days, weeks, or months) or with delivery of a bolus dose of drug over a relatively short period of time (*e.g.*, a few minutes to hours). The invention can also be used to irrigate a treatment site, *e.g.*, with disinfectant. Alternatively or in addition, the invention can be used as a sampling device, *e.g.*, by inserting a catheter through the guide that is connected to a vacuum source to withdraw fluid and/or tissue from the treatment site to facilitate diagnosis or prognosis of the subject.

Yet another advantage of the invention is that it can be used with any of a variety of drug delivery devices, including those that comprise an externally positioned drug release device or an implanted drug release device. The invention can also be used with drug delivery devices that comprise a drug delivery catheter, which catheter can be composed of a relatively permeable or relatively impermeable material. The invention is also amenable for use with a guide comprising relatively permeable or relatively impermeable material (*e.g.*, a relatively permeable guide can be used with a drug delivery device having a relatively impermeable drug delivery catheter, and a drug delivery device comprising a relatively permeable drug delivery catheter can be used with a relatively impermeable guide).

These and other objects, advantages and features of the present invention will become apparent to those skilled in the art upon reading this disclosure in combination with drawings wherein like numerals refer to like components throughout.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 is a cut-away view showing an exemplary guide 10 of the invention.

Fig. 2 is a cut-away view showing an exemplary drug delivery device 50 of the invention.

Fig. 3 is a cut-away view showing a guide 10 of the invention with a drug delivery device 50 inserted therein.

Fig. 4 is a cut-away view of a multi-lumen guide 10 having multiple drug delivery devices 50 stably positioned within the guide 10.

Fig. 5 is a cross-sectional view of a multi-lumen guide 10 with multiple drug delivery catheters 60 positioned therein.

Fig. 6 is a cross-sectional view of a single lumen guide 10 having two drug delivery catheters 60 positioned therein.

Figs. 7 and 8 are detailed, cut-away views of the distal end 62 of a drug delivery catheter 60 positioned within a guide 10 with a tapered distal end.

Figs. 9 and 10 are detailed, cut-away views of the distal end 62 of a drug delivery catheter 60 positioned within a guide 10 according to the invention.

Figs. 11 and 12 are illustrations of exemplary pre-set shapes for a guide.

Fig. 13 is a cut-away view of an exemplary alternative embodiment of the invention in which the proximal end of the guide is formed into a guide chamber 16, the distal end of which forms a partial cap over the proximal end of the drug delivery device and retains the drug delivery device within the guide 10.

Figs. 14 and 15 are detailed, cut-away views of the proximal end 11 of the guide showing various embodiments of the stable positioning element, which serves to stably position the drug delivery device within the guide 10.

Fig. 16 is a detailed, cut-away view of an alternative embodiment of the proximal end of a guide 10 of the invention.

Fig. 17 is a cut-away view of an exemplary alternative embodiment of the invention, where the proximal end of the guide provides a stable positioning element, and is associated with a distal portion of the drug release device.

Fig. 18 is a cut-away view of an exemplary alternative embodiment of the invention, where the proximal end of the guide provides a stable positioning element, and is associated with a distal portion of the drug release device.

Fig. 19 is a cut-away view of a guide 10 showing stable positioning of a drug delivery device within the guide 10 by removably attaching the guide proximal end 11 to a distal portion of a drug release device 70.

Fig. 20 is a perspective view of a drug delivery device 50 comprising a mechanical or electromechanical pump 75 as a drug release device (phantom-lined), where the drug delivery device is positioned for use within a guide 10.

Fig. 21 is an exploded view of Fig. 19 showing stable positioning of a drug delivery device by attachment of a drug release device 70 into a guide 10 using a snap-fit configuration.

Fig. 22 is a cut-away view of an exemplary alternative embodiment of the invention, illustrating the attachment of the drug delivery device to the guide by means of snap fit tab(s) of the drug delivery device inserted into snap fit recesses of the guide.

Fig. 23 is a cut-away view of an alternative embodiment for stable positioning of the drug delivery device 70 by attachment of a drug release device 70 into a guide 10 using a threaded male member 94.

Fig. 24 is an exploded view of a stable positioning element that stably positions the drug delivery device within a guide 10 by means of a threaded luer coupling member 96 that is threaded on to a threaded male portion 97 of a drug delivery device 70.

Fig. 25 is a cut-away view of a guide 10 having a self-sealing barrier element 25 positioned within a guide chamber 16.

Fig. 26 is a cut-away view of an exemplary drug delivery device 50 suitable for use with a guide of Fig. 25.

Fig. 27 is a cut-away view of an alternative embodiment of the drug delivery device illustrated in Fig. 26.

Fig. 28 is a cut-away view of an exemplary drug delivery device.

Fig. 29 is a cut-away view illustrating placement of a guide 10 using a tunneling device 85.

Fig. 30 is a cut-away view illustrating placement of a guide 10 into a tunneling device 85 using a wire 87 as reinforcement for pushing the guide 10 through the tunneling device 85.

Fig. 31 is a cut-away view illustrating a guide 10 comprising a reinforcing element channel 24 through which a wire 87 is introduced to facilitate placement of the guide.

Fig. 32 is a cross-section of the guide 10 and reinforcing element channel of Fig. 31.

Fig. 33 is a cut-away view of a drug delivery device 50 positioned within a guide 10, where the guide comprises sealing elements 28.

Figs. 34 and 35 are perspective and cut-away views, respectively, of a drug delivery device 50 positioned within a guide 10, where the stable positioning element is provided as a snap

fit tab 92 positioned in a wall of the guide 10, which snap fit tab 92 is seated within a snap fit tab recess 93 on the outer wall of the drug delivery device 50.

Fig. 36 is a perspective view of a drug delivery device 50 positioned within a guide 10, where the stable positioning element is provided as a luer lock composed of a tab 99 locked within a tab receiving slot 100.

Fig. 37 is a cut-away view of a guide 10 having a proximal end adapted for attachment to a guide chamber 16, where the guide is positioned within an insertion cannula 85.

Fig. 38 is a cut-away view of a guide 10 having a proximal end adapted for attachment to a guide chamber 16 and a guide chamber 16 attached by means of an attaching element 30.

Fig. 39 is cut-away view of a guide having a reinforcing element channel 24 with a closed distal end with a mandrel 110 positioned within the channel 24.

Fig. 40 is a cut-away view of a guide 10 having a reinforcing element channel 24 with a closed distal end, with a drug delivery device 50 positioned within the guide.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

Before the present drug delivery system, method of drug delivery, and specific devices and formulations used in connection with such are described, it is to be understood that this invention is not limited to the particular embodiments described, as such methods, devices, and formulations may, of course, vary. It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments only, and is not intended to limit the scope of the present invention which will be limited only by the appended claims.

It must be noted that as used herein and in the appended claims, the singular forms "a," "an," and "the" include plural referents unless the context clearly dictates otherwise. Thus, for example, reference to "a formulation" includes mixtures of different formulations, and reference to "the method of delivery" includes reference to equivalent steps and methods known to those skilled in the art, and so forth.

Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. Although any methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present invention, the preferred methods and materials are now described. All publications mentioned herein are incorporated herein by reference to disclose and describe the specific methods and/or materials in connection with which the publications are cited.

The publications discussed herein are provided solely for their disclosure prior to the filing date of the present application. Nothing herein is to be construed as an admission that the present invention is not entitled to antedate such publication by virtue of prior invention. Further, the dates of publication provided may be different from the actual publication dates which may need to be
5 independently confirmed.

Definitions

"Implantable" encompasses, but is not necessarily limited to, devices that can be substantially completely implanted within the body of a subject. For example, an "implantable"
10 device that is substantially completely implantable is one that is implanted at a subcutaneous site and, in some embodiments, extends to a site distal to the subcutaneous site (*e.g.*, to a treatment site located deeper within the subject's body).

"Controlled release" as used herein (*e.g.*, in the context of "controlled drug release") is meant to encompass release of substance (*e.g.*, a drug) at a selected or otherwise controllable rate,
15 interval, and/or amount. "Controlled release" thus encompasses, but is not necessarily limited to, substantially continuous delivery, patterned delivery (*e.g.*, intermittent delivery over a period of time that is interrupted by regular or irregular time intervals), and delivery of a bolus of a selected substance (*e.g.*, as a pre-determined, discrete amount of a substance, over a relatively short period of time (*e.g.*, a few seconds or minutes)).

20 The term "controlled drug release device" is meant to encompass any device that provides for controlled release of a drug or other desired substance and that can be adapted for use in the drug delivery device of the invention, *e.g.*, a drug delivery device that provides for controlled release of drug through a drug delivery catheter associated with the drug reservoir, and at a rate that is suitable to accomplish delivery of a therapeutically effective amount of drug to a treatment
25 site according to the methods of the invention.

The term "treatment site" as used herein is meant to refer to a desired site for delivery of drug from a drug delivery device of the invention, and/or a site from which sampling is desired, *e.g.*, for diagnosis and/or prognosis. "Treatment site" is thus meant to include, although is not necessarily limited to, a subcutaneous, intravenous, intrathecal, intraorbital, intraocular, intraaural,
30 intratympanic, intramuscular, intra-arterial, intra-articular, intracavitary, intraductal, intraglandular, intravascular, intranasal, intraperitoneal, intraspinal, epidural, intracranial, intracardial, intrapericardial, peritumoral, or intratumoral (*i.e.*, within a cancerous growth) site within a subject. "Treatment site" thus also encompasses intracavitary sites, *e.g.*, sites within or near a selected

organ or tissue (*e.g.*, central nervous system (*e.g.*, spinal fluid), kidney, liver, pancreas, heart (*e.g.*, intrapericardial), lung, eye, inner ear, middle ear, cochlea, lymph nodes, breast, prostate, ovaries, testicles, thyroid, spleen, *etc.*), into arteries that feed a selected organ to tissue, or at a site associated with a microbial infection (*e.g.*, bacterial, viral, parasitic or fungal infection).

5 The term "access site" or "implantation site" is used to refer to a site on or in a subject at which a guide and drug delivery device of the invention are introduced for implantation and positioning within the subject's body, *e.g.*, for delivery of drug to a desired treatment site. For example, where a guide is implanted in a subject for delivery of drug to the spinal cord, the access site or implantation site can be a subcutaneous site at which a proximal end of the guide is
10 substantially retained, and the treatment site is a position within or adjacent the spinal cord (treatment site) at which a distal end of the guide is positioned for delivery of drug.

"Drug delivery system" as used herein is meant to refer to a combination of a guide and drug delivery device of the invention suitable for use in delivery of a drug to a treatment site.

15 The term "subject" is meant any subject, generally a mammal (*e.g.*, human, canine, feline, equine, bovine, *etc.*), to which drug delivery is desired.

20 The term "impermeable" with reference to a dispensing device means that the material is sufficiently impermeable to environmental fluids as well as ingredients contained within the dispensing device such that the migration of such materials into or out of the device through the impermeable device is so low as to have substantially no adverse impact on the function of the device during the delivery period.

The term "semipermeable" means that the material is selectively permeable, *e.g.*, permeable to external fluids but substantially impermeable to other ingredients contained within the dispensing device and the environment of use.

25 The term "drug" as used herein is meant to encompass any substance suitable for delivery to a treatment site of a subject, which substances can include pharmaceutically active drugs, as well as biocompatible substances that do not exhibit a pharmaceutical activity in and of themselves, but that provide for a desired effect at a treatment site, *e.g.*, to flush or irrigate a treatment site (*e.g.*, saline).

30 "Pharmaceutically active drug," "therapeutic agent," "therapeutic drug," and the like are used interchangeably herein to refer to any chemical compound which, when provided to a subject, facilitates a therapeutic effect. Such drugs may optionally be provided in combination with pharmaceutically acceptable carriers and/or other additional compositions such as antioxidants, stable positioning agents, permeation enhancers, *etc.* Drugs compatible for delivery using the

devices and methods of the invention are discussed below, and are readily apparent to the ordinarily skilled artisan upon reading the disclosure provided herein.

The term "therapeutically effective amount" is meant an amount of a therapeutic agent, or a rate of delivery of a therapeutic agent, effective to facilitate a desired therapeutic effect. The
5 precise desired therapeutic effect will vary according to the condition to be treated, the drug to be administered, and a variety of other factors that are appreciated by those of ordinary skill in the art. Determinations of precise dosages are routine and well within the skill in the art.

The term "treatment" is used here to cover any treatment of any disease or condition in a mammal, particularly a human, and includes: a) preventing a disease, condition, or symptom of a
10 disease or condition from occurring in a subject which may be predisposed to the disease but has not yet been diagnosed as having it; b) inhibiting a disease, condition, or symptom of a disease or condition, *e.g.*, arresting its development and/or delaying its onset or manifestation in the patient; and/or c) relieving a disease, condition, or symptom of a disease or condition, *e.g.*, causing regression of the disease and/or its symptoms.

15

Overview of the Invention

The present invention, as it relates to an implantable drug delivery system, generally features: 1) an implantable guide comprising a proximal end, a distal end, and a wall defining a lumen; and 2) a drug delivery device minimally comprising a drug release device that can be
20 implantable within the body or left external from the body and, in a preferred embodiment, further comprises a drug delivery catheter. The guide can be substantially permanently implanted within a subject to provide a conduit to a desired treatment site (*e.g.*, a body tissue, organ, or other site). The drug delivery device is then stably positioned within the guide to provide for delivery of drug from the drug delivery device to the treatment site. Preferably, the drug delivery device is
25 retrievable or replaceable, *e.g.*, the drug delivery device can be removed from the guide and, where desirable, another drug delivery device inserted in its place, and can be completely or partially implanted, or completely or partially external to the subject.

In one embodiment, the drug delivery device comprises a drug delivery catheter, which provides for delivery of drug from a drug reservoir to the treatment site. In this embodiment, the
30 drug delivery catheter of the drug delivery device is threaded through the guide so that the drug delivery outlet of the drug delivery catheter is positioned for delivery of drug at the treatment site. At least a portion of the drug delivery device is retained at an accessible access site (*e.g.*, the drug release device portion of the drug delivery device is retained at a subcutaneous access site). In

another embodiment, the drug delivery device comprises a leash for retrieving the drug delivery device. Drug delivery devices comprising a leash can be positioned at any point within the lumen of a guide (*e.g.*, at a site any distance from a subcutaneous access site at which the drug delivery device is initially introduced into the guide). In this latter embodiment, the drug delivery device
5 can further comprise a drug delivery catheter, although such may not be necessary.

After delivery of the drug from the drug delivery device is complete (*e.g.*, the drug reservoir is substantially empty) or it is otherwise desirable to terminate delivery of drug, the drug delivery device can be removed from the guide without losing access to the treatment site, *i.e.*, access to the treatment site is maintained by the guide. The guide thus facilitates removal and
10 replacement of the drug delivery device through the same conduit or treatment site access route, without the need to re-establish access the treatment site. Furthermore, the guide and drug delivery device system of the invention allows for exchange and replacement of the drug delivery device without the need to uncouple the drug release device from a drug delivery catheter, thus substantially reducing both the risk of leakage of drug from the device and the risk of
15 contamination of the treatment site (*e.g.*, by introduction of contaminants into the drug delivery catheter). In addition, the drug delivery catheter of the drug delivery device can be coated with silver or otherwise coated or treated with antimicrobial agents, thus further reducing the risk of infection at the treatment site. The entire drug delivery system can be implanted within the subject, and can be provided in a size and configuration that minimizes discomfort or
20 inconvenience to the subject. In addition, all or a portion of the drug delivery device can be retained outside the subject with the drug delivery catheter residing in the guide.

The specific components of the guide and exemplary drug delivery device suitable for use with the guide will now be described in further detail and in relation to the drawings provided herein. The specific components and embodiments of the invention provided below are not meant
25 to be limiting, but rather only illustrative of the claimed invention. For example, while the drug delivery device is illustrated as comprising a controlled drug release device that is an elongate cylinder, and/or the guide is generally illustrated as comprising a stable positioning element that stably positions a drug delivery device within the guide, (*e.g.*, a guide chamber that is of a shape suitable for receiving a drug release device), other forms and types of controlled drug release
30 devices, as well as other forms and variations of the guide, are suitable for use in invention. Moreover, while an osmotic pump is a preferred form of controlled drug release device, other controlled drug release devices are also suitable for use in the drug delivery device and guide of the invention, and thus are contemplated by and within the scope of the present invention.

Guide

In general, the guide comprises a proximal end, a distal end, and a body defining at least one lumen. Typically the guide is provided as an elongated, substantially hollow tube. In one embodiment, the guide further comprises a stabilizing element, which facilitates retention and/or positioning of all or at least a portion of a drug delivery device within the guide, *e.g.*, as during use in drug delivery to a treatment site. Fig. 1 illustrates an exemplary embodiment of the guide 10 of the invention, in which the guide is provided in a substantially hollow, cylinder-type configuration comprising a guide body 20 defining a guide lumen 13, and a stable positioning element, which in this embodiment is exemplified by a guide chamber 16. The guide chamber 16, as well as further exemplary stable positioning elements, are described in more detail below. In the embodiment provided in Fig. 1, the guide chamber 16 is designed to receive and, preferably, retain a drug delivery device 50, generally through reversible association of a drug release device 70 and the guide chamber 16. The guide body 10 further comprises distal and proximal ends 21 and 22. The distal end of the guide chamber 16 defines an opening 17 that is in communication with the lumen of the guide body 20. As illustrated in Fig. 3, the guide is suitable for use with a drug delivery device 50, which in this example comprises a drug delivery catheter 60 threaded through the guide chamber 16, through opening 17, and into the lumen of the guide body 20.

The guide need not comprise a septum or other element that substantially covers the proximal end 11 of the guide when the guide is used in conjunction with a drug delivery device, since access to the guide lumen from the guide proximal end will generally be inhibited or substantially unavailable when a drug delivery device is positioned within the guide (*e.g.*, due to the communication of the drug delivery device, the guide, and a sealing element positioned between an outer wall of the drug delivery device and an inner wall of the guide. Where it is desirable to leave the guide implanted without a drug delivery device in position within the guide, it may be desirable to cap or otherwise temporarily or reversibly close the open proximal end of the guide, *e.g.*, to prevent accumulation of fluids or other biomaterial in the guide and/or to inhibit tissue growth into or within the guide.

The guide of the invention can be designed for use with a single drug delivery device, or can be designed for use with a plurality (*e.g.*, two or more) drug delivery devices. Fig. 4 illustrates an exemplary guide 10 that is designed for use with two drug delivery devices 50. The drug delivery devices 50 can be stably positioned for use in the guide 10 by any suitable means (*e.g.*, press-fit lock, threaded element, bayonet connector, *etc.*). The guide 10 can have a plurality of lumen 13 wherein a drug delivery catheter 60 can be positioned within at least one of the lumen

(see, *e.g.*, Fig. 5). Alternatively, the guide 10 has a single lumen 13 into which a plurality of drug delivery catheters 60 are introduced (see, *e.g.*, Fig. 6).

The guide 10 can be made of any suitable biocompatible material. Exemplary materials include, but are not necessarily limited to, polymers; metals; glasses; polyolefins (high density polyethylene (HDPE), low density polyethylene (LDPE), linear low density polyethylene (LLDPE), polypropylene (PP), and the like); nylons; polyethylene terephthalate; silicones; urethanes; liquid crystal polymers; PEBAX™; HYTREL™; TEFLON™; perfluoroethylene (PFE) perfluoroalkoxy resins (PFA); poly(methyl methacrylate) (PMMA); multilaminates of polymer, metals, and/or glass; and the like. The guide can be made of the same materials throughout its length, or may vary in composition over its length.

The guide may comprise a reinforcement element(s) to provide for enhanced stiffness, to avoiding kinking of the guide body, *etc.* The reinforcement element(s) can be, for example, a coil or braid that is on the outer surface of the guide body, within a wall of the guide body, or positioned on the inner wall of the guide body. The guide 10, as well as other guide components (*e.g.*, a stable positioning element for stably positioning a drug delivery device within the guide), can be made of the same or different materials, and may be manufactured as a single piece (*e.g.*, by molding) or as separate pieces that are subsequently attached one to another using any suitable attachment means.

The material(s) of the guide 10, and particularly of the guide body 20, are generally selected so that the guide is sufficiently flexible to facilitate insertion and placement at the treatment site. The guide can be of substantially the same degree of flexibility or stiffness throughout its length, or may vary in flexibility or stiffness over its length (*e.g.*, a distal portion of the guide body may be more or less flexible than a proximal portion of the guide body). The desired flexibility or stiffness of the guide can be varied with the particular treatment site and/or drug delivery pathway with which the guide is to be used. For example, where the drug delivery pathway is defined in whole or in part by one or a series of biologically defined lumen (*e.g.*, vein artery, capillary, lymphatic, organ duct (*e.g.*, duct of a secretory gland (*e.g.*, salivary gland, liver, pancreas, *etc.*)), and the like), it may be desirable to use a guide having flexibility sufficient to conform the guide to the biological pathway, *e.g.*, the guide is flexible enough to be deflected by the walls of the biologically defined lumen into which it is introduced. Alternatively, where the drug delivery pathway may be defined as a site deep within a tissue, it may be desirable to select a guide having at least a relatively stiff portion to facilitate placement of the guide. However, the use

of relatively stiff guides can be avoided where a tool such as a trocar, guidewire, or other device is used to facilitate implantation.

The dimensions of the guide 10, particularly the guide body 20 and any other elements or components of the guide, can be varied depending upon a variety of factors, such as the particular treatment site to which drug delivery is desired, the access route used to reach the desired treatment site, the dimensions of the components of the drug delivery device (*e.g.*, the dimensions of the drug release device or drug delivery catheter) to be used with the guide, *etc.* For example, in the exemplary embodiment depicted in Fig. 1, the inside diameter of the guide chamber 16 and of the guide body 20 will generally be sufficiently greater than the outside diameter of the drug release device and drug delivery catheter, respectively, so that the drug delivery device can be reversibly threaded into the guide and retained within the guide while implanted.

In general, the guide body 20 will typically have a length in the range from about 1 cm to 150 cm, usually having a length in the range from about 2-5 cm up to about 50 cm. The outside diameter of the guide body that defines the lumen in which the drug delivery device resides will typically be in the range from about 0.1 mm (0.3 F) or 0.15 mm and up to about 2 mm (6 F) or 2.5-3 mm, usually being in the range from about 0.125 mm (0.4 F) to about 1 mm (3 F). In one embodiment, the guide an outer diameter of about 0.020". The inner diameter of the guide is generally in the range from about 0.025 mm-0.03 mm to about 1.5-2 mm, usually being in the range from about 0.05 mm to 1 mm. Normally guides comprising a guide body having larger outside diameters usually having larger lumen diameters. In one embodiment, the guide body has an inner diameter of about 0.035".

In general, the guide body length ranges from about 1 cm to about 200 cm, usually from about 15 cm to about 40 cm; an outside diameter in the range from about 0.125 mm (0.4 F) to about 3 mm, usually from about 0.66 mm (2 F) to about 0.5 mm; and an inside diameter in the range from about 0.05 mm to about to about 2 mm, usually from about 0.075 mm to about 0.5 mm (2 F). The inside diameter of the guide body is generally greater than the outside diameter of a drug delivery catheter and/or drug delivery device that is to be used in conjunction with the guide.

The dimensions of the guide can vary according to a variety of factors, *e.g.*, the dimensions of the drug delivery device with which the guide is to be used, the treatment site, the material of the guide, *etc.* For example, where the guide body is comprised of a material that has elastic qualities, the guide body may have an inside diameter that is smaller than or equal to the outside diameter of the drug delivery device or a position thereof. Upon insertion of the drug delivery

device, the guide expands or stretches to accommodate insertion of the drug delivery device into the guide lumen.

In addition to the uses described herein in drug delivery, the guide of the invention can also be used as a conduit for other purposes. For example, the guide can be used in conjunction with a sampling device, *e.g.*, a vacuum source can be attached to a catheter, which is threaded through a lumen of a guide to the treatment site. The sampling device positioned within a guide of the invention can be used to extract a biological sample (*e.g.*, biological fluids (*e.g.*, blood, spinal fluid, lymph, *etc.*), cells, tissue, *etc.*) from a treatment site. Other uses of the guide, drug delivery device, and drug delivery system of the invention will be readily apparent to the ordinarily skilled artisan upon reading of the disclosure provided herein, and as such are contemplated and encompassed by the present invention.

Exemplary embodiments of guides contemplated and within the scope of the invention are described in more detail below.

Guide body

In one embodiment, the body 20 of the guide 10 is provided as a substantially hollow tube. The guide body 20 is designed so as to facilitate the placement of the drug delivery catheter 60 of a drug delivery device 50 of the invention through the conduit created by the lumen of the guide body 20, thus providing for delivery of drug from the distal end 61 of the drug delivery catheter 60 to the treatment site. The distal end 12 of the guide 10 can be provided in any of a variety of configurations. For example, the distal end 12 may be provided in a closed configuration, such that the inner diameter of the distal end 12 is less than the diameter of the proximal portion of the guide body 20, but greater than the outer diameter of the distal end 62 of the drug delivery catheter 60 (Fig. 7).

In one embodiment, the distal end 12 of the guide body 20 comprises a valve, *e.g.*, a duckbill valve, that is forced open upon insertion of the drug delivery catheter distal end 62 into the guide distal end 12 (Fig. 8). In this "closed" configuration, drug may be delivered from the drug delivery catheter distal end through the tip of the guide distal end 12, thus avoiding insertion of drug delivery catheter directly into the treatment site. This latter embodiment may be particularly advantageous where, for example, the drug delivery catheter is made of a relatively stiff material and/or may have a sharp end that may damage tissue at the treatment site. This embodiment may also be particularly advantageous where the treatment site is particularly sensitive. Moreover, providing a valve at the guide distal end 12 can help the clinician or other operator implanting the device from inserting a drug delivery device having a drug delivery catheter that is too long for use

with the guide implanted in the patient, thus avoiding insertion of the drug delivery catheter into tissue beyond the distal end of the guide.

Where desired, the length of the drug delivery catheter 60 relative to the length of the guide body 20 may be varied. For example, the catheter 60 can be of a length such that the distal end 62 of the catheter 60 is at a point beyond the distal end 12 of the guide 10 (Figs. 7 and 9) or at a point within the distal end 12 of the guide 10 (Figs. 8 and 10). When the guide distal end 12 is provided as the closed distal end embodiment as depicted in Fig. 8 and the catheter distal end 62 is seated within the guide distal end 12, drug is delivered through the catheter 60 and out of the tip of the guide 10. Where the guide distal end 12 is provided as the open distal end embodiment as depicted in Fig. 10 and the catheter distal end 62 is seated within the guide distal end 12, drug may diffuse in all directions within the guide lumen, including out the guide distal end 12.

The guide 10 can be modified as may be suitable for particular uses, *e.g.*, as may be required or optimal for use for drug delivery to various treatment sites. For example, the guide can comprise coatings such as hydrophilic, anti-thrombogenic, low-friction, or hydrophobic coatings, which can be placed over the inner or outer surface of the guide body. Additionally, the distal end of the guide can be formed into a desired geometry, as described above, and the strength and flexibility characteristics of the guide body can be further modified by varying the materials used in the manufacture of the guide. For example, the guide can be multi-laminate with a biocompatible outer surface and a lubricated lining. As described for the drug delivery catheter, the guide can be formed into a pre-set shape or geometry to facilitate insertion and/or drug delivery to at desired treatment site.

The guide can be made from a material or matrix of materials (*e.g.*, reinforced construction with braided wire, coiled, wire, etc.) or can be formed from multiple layers of materials. The guide body can be formed into any of a variety of pre-set shapes, which may be particularly desirable to facilitate access to a particular treatment site. For example, particular pre-set shapes are useful to facilitate delivery of drug through a coronary artery of the right or left side of the heart. Furthermore, particular guide shapes may be desired for use in drug delivery to treatment sites such as the spine, inner ear, pericardial space, or a location within an organ (*e.g.*, to delivery drug to a tumor of a selected organ). Exemplary pre-set guide body shapes useful in delivery of drug to via a coronary artery include, but are not limited to, those shown in Fig. 11 (hockey stick) and Fig. 12 (amplatz shape).

The guide 10 can be further modified by providing radiopaque markers 18 at one or more locations along its length. In one embodiment, radiopaque markers are provided at the tip of the

guide distal end (Figs. 9 and 10). Such radiopaque markers can comprise metal rings (*e.g.*, platinum, palladium, gold, *etc.*), or can be defined by impregnating the body of the guide with appropriate radiopaque dyes or other radiopaque materials. The provision of radiopaque markers is well known in the art.

5 Positioning and/or retention of a drug delivery device within a guide

In one embodiment, the guide comprises a stable positioning element. The stable positioning element is any element that facilitates association or coupling of a drug delivery device with a guide, *e.g.*, as during use in drug delivery to a treatment site. For example, where the drug delivery device does not comprise a drug delivery catheter, the stable positioning element stably
10 positions all or a substantial portion of the drug release device of the drug delivery device within the guide lumen. Where the drug delivery device comprises a drug delivery catheter, the stable positioning element stably positions at least a portion of the drug delivery catheter within the guide, and further preferably stably retains or positions the drug release device of the drug delivery device immediately adjacent the guide proximal end (*i.e.*, such that the drug release device communicates
15 with at least a portion of the guide proximal end) or stably retains or positions substantially all or a portion of the drug release device within the guide lumen. Any of a variety of such means are compatible for use in the drug delivery system of the invention. Non-limiting examples of such means are provided below.

In one exemplary embodiment, illustrated in Figs. 1 and 3, the guide 10 comprises a guide
20 chamber 16 as the stable positioning element. In this embodiment, the guide chamber 16 of guide 10 is designed for receiving and positioning the drug release device 70 of the drug delivery device 50. To this end, the guide chamber 16 and/or the drug delivery device that is to be positioned within the guide chamber 16 can be designed to facilitate retention of the drug delivery device within the guide chamber 16. The walls of the guide chamber 16 can completely encompass the
25 drug release device of the drug delivery device (as exemplified in Fig. 3), or can be of any length sufficient to accomplish stable positioning, and preferably retention, of the drug delivery device within the guide so that drug is delivered from the drug delivery device to the treatment site. The guide chamber 16 can comprise additional elements to accomplish retention of the drug delivery device within the guide, such as an end cap portion that is permanently or removably attached to a
30 distal end of the guide, and which can cover the proximal end of the guide (see, *e.g.*, Fig. 13).

In another example, the stable positioning element is provided as a "locking/docking" mechanism. Examples of such locking/docking mechanisms that can serve as are provided in Figs. 14-16. In one embodiment, the proximal end 11 of the guide 10 is in the form of a press-fit

lock 90, so that upon insertion of the drug delivery device 50 into the guide 10, the body of the drug release device 70 of the drug delivery device 50 is held in place by force of the walls of the guide chamber 16 (Fig. 14). Preferably, a vent 89 is provided to allow escape of any fluid within the guide chamber 16 upon pressing the drug release device 70 into place.

5 Alternatively, the drug delivery device comprises a stable positioning element that can interact with, for example, a proximal end of the guide. For example, as illustrated in Fig. 15, a distal portion of the drug delivery device 50 forms a flanged end cap portion 91 that, when the drug delivery device 50 is seated within the guide 10, overlays the guide proximal end 11 and retains the drug delivery device 50 within the guide 10. In this latter embodiment, the proximal
10 end of the guide can be fashioned from compressible material, so that the proximal end can be depressed, the drug delivery device with a flanged-end cap portion positioned within the guide, and the proximal end released so that the wall of the distal end presses against the inner side of the flanged end cap of the drug delivery device.

 In another embodiment, the locking/docking mechanism is provided by attachment of the
15 guide proximal end 11 to a distal portion of the drug delivery device 50, *e.g.*, by means of a press fit lock 90 (see, *e.g.*, Figs. 16, 17, and 18). Other exemplary locking/docking mechanisms suitable for use in the invention include, but are not necessarily limited to, bayonet style connectors, thread connectors (*e.g.*, where the proximal end of the release device is provided with a threaded cap that overlays and threads onto a threaded portion of the guide distal end), and various retaining means
20 known in the art.

 Alternatively, the stable positioning element is designed from a proximal end of the guide to provide for association of the guide with a distal portion of a drug release device of the drug delivery device. For example, as illustrated in Figs. 19 and 20, the proximal end 11 of the guide
25 10 can be fashioned so as to be removably attached to a distal end portion of a drug release device 70. The drug release device 70 can be secured within the guide proximal end by means of insertion of a snap fit tab 92 into a snap fit recess 93. For example, the snap fit tab 92 portion can be positioned at the distal end of the drug release device 70 and mate with a snap fit recess 93 at a proximal end 11 of the guide 10 (see, *e.g.*, Figs. 21 and 22). In one preferred embodiment, the snap fit tab 92 portion is positioned on the guide (*e.g.*, as a portion of a guide chamber) and mates
30 with a snap fit recess 93 on the outer surface of the drug release device 70 of the drug delivery device 50 (see, *e.g.*, Figs. 34 and 35). The snap fit recess 93 can be fashioned as a circumferential recess around the outer diameter of a portion of the drug release device 70. Alternatively, a

threaded male member 94 can be provided at the distal end of the release device 70 and threaded into a threaded recess 95 within the proximal end 11 of the guide 10 (see Fig. 23).

In another embodiment, the proximal end 11 of the guide 10 is provided with a threaded luer coupling member 96 (exemplified by a female luer lock) that is threaded on to a threaded male portion 97 of a drug delivery device 70 (see, *e.g.*, Fig. 24). Preferably, the threaded coupling member 96 can be threaded onto the threaded male portion 97 by manipulation of substantially only the threaded coupling member 96, thus avoiding further manipulation of the drug delivery device 50. In one preferred embodiment, the lock is provided as a bayonet style connector provided as a tab 99 positioned on a proximal portion of the drug delivery device 50, where the tab 99 is received by a tab receiving slot 100 positioned at a proximal end of the guide 10 (see, *e.g.*, Fig. 36).

In still another embodiment, the guide 10 comprises a self-sealing barrier element 25 positioned at a proximal end of the guide 10 (see, *e.g.*, Fig. 25). The self-sealing barrier element 25 may be cross-linked by a hydrophobic polymer. In use, a drug delivery device 50 comprising a drug delivery catheter 60 having a relatively sharp distal end 62 (see, *e.g.*, Figs. 26 and 27) is inserted into the guide 10 so that the sharp distal end 62 pierces the self-sealing barrier element 25. The drug delivery device 50 is stably positioned within the guide by virtue of the self-sealing barrier element 25, which also provides for isolation of at least a portion of the guide lumen 13 from the environment during implantation of the drug delivery device 50. As such the self-sealing barrier element 25 must be of a thickness sufficient to inhibit movement of the drug delivery device within and/or out of the guide lumen.

Alternatively or in addition, the drug delivery device and/or guide can be anchored at an external or internal site with respect to the subject by any suitable conventional means. For example, sutures can be used to secure the drug delivery device proximal end at or near an implantation site. The guide can be similarly be anchored within the subject.

Sealing elements

In one embodiment, the guide 10 comprises a sealing element 28 (see, *e.g.*, Fig. 33). In general, the sealing element 28 is positioned within the guide lumen so as to prevent bodily fluids from the target tissue 45 and drug delivered from a drug delivery device 50 positioned within the guide 10 from flowing back into the guide 10. The sealing element 28 can be manufactured from any suitable material that is substantially non-reactive with bodily fluids or tissue and substantially non-reactive with the drug formulation to be delivered using the system of the invention. For example, the sealing element material can be a soft, resilient, self-lubricating elastomeric material,

such as silicone rubber. The sealing element can be provided as a separate element that is attached to the guide inner wall, or may be a continuous extension of the material of the guide inner wall. In addition to providing a liquid-proof seal, one sealing element or a plurality of sealing elements can also serve to stably position a drug delivery device within the guide.

5 In one embodiment, the sealing element is a ring-like structure, where the outer diameter of the sealing element is associated with the inner wall of the guide. The sealing element defines a central passage through which the drug delivery device is removably inserted. The central passage is preferably of a size sufficiently large to accommodate insertion of the drug delivery device without tearing or otherwise damaging the sealing element or damaging the drug delivery device,
10 but sufficiently small so that, following insertion of the drug delivery device, a substantially liquid-tight seal is formed between the sealing element inner surface and the portion of the drug delivery device with which the sealing element communicates. The sealing element may contain or be coated with materials to facilitate smooth insertion and removal of the drug delivery device.

 The sealing element (*e.g.*, the inner surface of the sealing element passage) can be shaped
15 to facilitate insertion of the drug delivery device and/or to accommodate the shape of the drug delivery device portion with which it communicates. For example, the sealing element inner surface can be beveled to receive a portion of the drug delivery device, so that the drug delivery device is seated within the sealing element inner surface wall. In another example, the body of the sealing element can taper in thickness toward the central passage, *e.g.*, the sealing element body is
20 thicker where it communicates with the guide and is relatively thinner at the edge of the central passage. In this latter embodiment, the tapered sealing element can be designed to flex upon insertion of the drug delivery device, so that a portion of a side wall of the sealing element contacts a portion of the drug delivery device, providing an increased area of contact between the sealing element and the drug delivery device.

25 As exemplified in Fig. 33, the guide 10 can comprise a plurality of sealing elements 28, and can be positioned at various points within the guide lumen. In one embodiment, the guide comprises at least one sealing element positioned within a distal portion of the guide lumen, *e.g.*, so as to provide a liquid-proof seal with a drug delivery catheter 60 positioned within the guide lumen. The sealing element can be positioned, for example, at or near the extreme distal end of
30 the guide. The size of the outer diameter and dimensions of the central passage are varied according to the dimensions of the guide 10 and drug delivery device 50.

 The sealing element design can also be varied according to the implantation methods used and the treatment site to be accessed. For example, the guide can be implanted with the drug

delivery device positioned within the guide, so that the sealing elements provides a liquid-proof seal during implantation. Alternatively, the guide can be implanted prior to insertion of the drug delivery device. In this latter method, it may be desirable to provide the guide with one or more sealing elements that inhibit flow of bodily fluids into the guide during implantation. For example, the guide can comprise a sealing element positioned within a distal portion of the guide lumen, where the sealing element is designed to substantially inhibit flow of bodily fluids or other liquids into the guide. Exemplary sealing elements that can facilitate inhibition of liquid entry into the guide lumen include sealing elements that define a relatively small central passage. In this embodiment, the sealing element is designed of a flexible material or is tapered in thickness toward the central passage to allow for insertion of a drug delivery device. Alternatively, the self-sealing element may comprise a central passage that is not simply empty space, but rather comprises a self-sealing material, *e.g.*, the self-sealing material is positioned within at least a central portion of the sealing element. The self-sealing material positioned within the sealing element central passage is such that a drug delivery device can be readily inserted through the sealing element central passage and, upon withdrawal of the drug delivery device, re-seals to substantially inhibit flow of liquid into the guide lumen. The distal end of the drug delivery device (*e.g.*, the distal end of the drug delivery catheter) can be fashioned for use with such self-sealing sealing elements (*e.g.*, by providing the drug delivery catheter with a tapered or sharpened distal end).

Drug Delivery Device

The drug delivery device 50 minimally comprises a drug release device 70 and, in a preferred embodiment, further comprises and a drug delivery catheter 60 (see, *e.g.*, Figs. 2 and 28). The proximal end 61 of the drug delivery catheter 60 is attached to the drug release device 70 so that the lumen of the drug delivery catheter 60 is in communication with an orifice 73 such that drug contained in the reservoir 74 can move through orifice 73 and into the drug delivery catheter 60 and out the tip of the drug delivery catheter distal end 62.

In an alternative embodiment, the drug delivery device comprises a leash that facilitates retrievable positioning of the drug delivery device at any site within the lumen of the guide. In this latter embodiment, the drug delivery device may further comprise a drug delivery catheter.

Each of the components of the drug delivery device will now be described in more detail.

Drug release device

The drug delivery device of the invention can be designed for use in conjunction with any of a variety of drug release devices. In general, the drug release devices suitable for use in the invention comprise a reservoir 74, which reservoir retains a drug formulation therein. The drug release device can be selected from any of a variety of conventional drug release devices that are conventionally used as an external element (*e.g.*, an external pump) or implanted element of a drug delivery system. In a preferred embodiment, the drug release device is a controlled drug release device. Controlled drug release devices suitable for use in the present invention generally can provide for delivery of the drug from the reservoir 74 at a selected or otherwise patterned amount and/or rate through a drug delivery catheter 60 and to a treatment site in the subject.

Release of drug from the reservoir, particularly controlled release of drug from the reservoir, can be accomplished in any of a variety of ways according to methods well known in the art, *e.g.*, by incorporation of drug into a polymer that provides for substantially controlled diffusion of drug from within the polymer, incorporation of drug in a biodegradable polymer, providing for delivery of drug from an osmotically-driven device, *etc.* Drug can be delivered through the drug delivery catheter to the treatment site as a result of capillary action, as a result of pressure generated from the drug release device, by diffusion, by electrodiffusion or by electroosmosis through the device and/or the catheter.

The reservoir 74 of the drug release device 70 is preferably made of an impermeable material that is sufficiently strong to ensure that it will not leak, crack, break or distort so as to expel its active agent contents under stresses it would be subjected to during use, *e.g.*, due to physical forces exerted upon the drug release device as a result of movement by the subject or physical forces associated with pressure generated within the reservoir associated with drug delivery through the drug delivery catheter. Reservoir 74 must also be chemically inert (*e.g.*, does not react with the active agent formulation) and is preferably biocompatible (*e.g.*, where the device is implanted, it is substantially non-reactive with respect to a subject's body or body fluids).

Suitable materials for reservoir 74 generally comprise a non-reactive polymer or a biocompatible metal or alloy. Suitable polymers include, but are not necessarily limited to, acrylonitrile polymers such as acrylonitrile-butadiene-styrene polymer, and the like; halogenated polymers such as polytetrafluoroethylene, polychlorotrifluoroethylene, copolymer tetrafluoroethylene and hexafluoropropylene; polyimide; polysulfone; polycarbonate; polyethylene; polypropylene; polyvinylchloride-acrylic copolymer; polycarbonate-acrylonitrile-butadiene-styrene; polystyrene; and the like. Further exemplary polymers are described in The Handbook of

Common Polymers, Scott and Roff, CRC Press, Cleveland Rubber Co., Cleveland, Ohio. Metallic materials suitable for use in the reservoir 74 of the drug release device 70 include stainless steel, titanium, platinum, tantalum, gold and their alloys; gold-plated ferrous alloys; platinum-plated titanium, stainless steel, tantalum, gold and their alloys as well as other ferrous alloys;

5 cobalt-chromium alloys; and titanium nitride-coated stainless steel, titanium, platinum, tantalum, gold, and their alloys.

A reservoir made from titanium or a titanium alloy having greater than 60%, often greater than 85% titanium is particularly preferred for the most size-critical applications, for high payload capability and for long duration applications and for those applications where the formulation is
10 sensitive to body chemistry at the implantation site or where the body is sensitive to the formulation. Preferred reservoir materials maintain at least 70% active agent after 14 months at 37°C and have a shelf stability of at least about 9 months, or more preferably at least about two years, at about 2°C to 8°C. Most preferably, the drug delivery devices are designed for storage with drug at room temperature. Where unstable formulations are in reservoir 74, *e.g.*, protein
15 and/or peptide formulations, the metallic components to which the formulation is exposed are preferably formed of titanium or its alloys as described above.

Drug release devices suitable for use in the drug delivery devices of the invention may be based on any of a variety of drug delivery systems. For example, the drug release device can be based upon a drug diffusion system, *e.g.*, where the drug is incorporated into a polymer, and the
20 polymer is provided within a drug-impermeable reservoir 74 that is communication with a drug delivery catheter 70. In one embodiment, the polymer provides for release of drug concomitant with degradation of a drug-impregnated polymeric material (*e.g.*, a biodegradable, drug-impregnated polymeric material). In other embodiments, the drug release device is accomplished by osmotic pumps, electrodiffusion, electroosmosis, vapor pressure pumps, electrolytic pumps,
25 effervescent pumps, piezoelectric pumps, erosion-based systems, diffusive systems, *etc.*

Controlled release of drug can be accomplished by the design of the drug formulation present in the drug delivery device (*e.g.*, within the drug delivery device reservoir or within the drug delivery catheter), the design of the drug release device, and/or the design of the drug delivery catheter. For example, the catheter can be loaded with polymer that provides for
30 controlled diffusion of drug from the drug reservoir.

Drug release devices based upon a mechanical or electromechanical infusion pump, are also suitable for use with the present invention. Examples of such devices include those described in, for example, U.S. Pat. Nos. 4,692,147; 4,360,019; 4,487,603; 4,360,019; 4,725,852, and the

like. In general, the present invention can be used in conjunction with refillable, non-exchangeable pump systems. In this latter context the present invention provides several advantages, including improved and repeated access to a treatment site, as well as the elimination of fluid coupling issues normally associated with the conventional use of such devices.

5 In one embodiment, the drug release device is a controlled drug release device in the form of an osmotically-driven device. Preferred osmotically-driven drug release systems are those that provide for release of drug at a rate of about 0.01 $\mu\text{g/day}$ to about 100 mg/day , which drug can be delivered at a volume rate of from about 0.01 $\mu\text{l/day}$ to about 100 $\mu\text{l/day}$, preferably about 0.04 $\mu\text{l/day}$ to about 10 $\mu\text{l/day}$, generally about 0.2 $\mu\text{l/day}$ to about 2.0 $\mu\text{l/day}$. Exemplary
10 osmotically-driven devices suitable for use in the invention include, but are not necessarily limited to, those described in U.S. Pat. Nos. 3,760,984; 3,845,770; 3,916,899; 3,923,426; 3,987,790; 3,995,631; 3,916,899; 4,016,880; 4,036,228; 4,111,202; 4,111,203; 4,203,440; 4,203,442; 4,210,139; 4,327,725; 4,627,850; 4,865,845; 5,057,318; 5,059,423; 5,112,614; 5,137,727; 5,234,692; 5,234,693; 5,728,396; and the like.

15 In one embodiment the controlled drug release device is an osmotic pump, *e.g.*, an osmotic pump similar to that described in U.S. Pat. No. 5,728,396. In one embodiment of particular interest, the osmotic pump is a DUROSTM osmotic pump. In general, osmotic pumps operate by imbibing fluid from the outside environment and releasing corresponding amounts of the therapeutic agent. The reservoirs of osmotic pumps can be a single chamber, or can be divided
20 into two chambers (*e.g.*, a piston can separate the two chambers). Where the pump comprises two chambers, the first chamber (which lies within one portion of the drug release device reservoir) contains a fluid-imbibing agent, and the second chamber (which lies within a second portion of the drug release device reservoir) contains a therapeutic agent. The fluid-imbibing agent in the first chamber is isolated from the active agent in the second chamber. Where a piston serves to
25 separate the two chambers, the piston is capable of sealably moving under pressure within the reservoir.

A back-diffusion regulating outlet defines an end of the drug-containing second chamber of the osmotic pump. An exemplary back-diffusion regulating outlet is one based on a male threaded member in a mating relationship with the smooth interior surface of the reservoir wall
30 defining the sidewalls of the first chamber, which threaded member forms a helical flow path between the mating surfaces of the back-diffusion regulating outlet and the reservoir through which therapeutic agent from the second chamber can flow. The pitch, the amplitude, and the cross-sectional area and shape of the helical path formed are factors that affect both the efficiency

of path preventing back-diffusion of external fluid into the second chamber and the back pressure in the device. The geometry of outlet also prevents water diffusion into the reservoir. In general, the characteristics of the flow path are selected so that the length of the helical flow path and the velocity of flow of active agent therethrough is sufficient to prevent back-diffusion of external fluid through the flow path without significantly increasing the back pressure, so that the release rate of the active agent is primarily governed by the osmotic pumping rate. Alternatively or in addition, where the drug delivery device comprises a drug delivery catheter, the drug delivery catheter can be designed to serve as a back diffusion regulating element.

The first chamber comprises a water-swellaable semipermeable membrane. The material of the semipermeable membrane is selected so that it is capable of imbibing between about 0.1% and 200% by weight of water. The semipermeable membrane imbibes fluid to generate a force transferable to the drug-containing second chamber of the pump, thus forcing drug within the second chamber out of the orifice of the second chamber at a controlled rate. The polymeric materials from which the semipermeable membrane may be made vary based on the pumping rates and a device configuration requirements and include but are not limited to plasticized cellulosic materials, enhanced polymethylmethacrylate such as hydroxyethylmethacrylate (HEMA) and elastomeric materials such as polyurethanes and polyamides, polyether-polyamide copolymers, thermoplastic copolyesters and the like.

Drug Delivery Catheter

The drug delivery catheter 60 is generally an hollow tube having a proximal end 61 associated with the drug release device 70 and a distal end 62 for delivery of drug to a desired treatment site. The drug delivery catheter 60 can be provided as an extended orifice from the drug release device 70, *e.g.*, the catheter 60 can be extruded from the body of the drug release device 70 itself so that the catheter is an extension of the material of the wall of the drug release device. Alternatively, the drug delivery catheter can be provided as a component separate from the body of the drug release device 72, which is attachable to the drug release device to, for example, provide for flow of drug through orifice 73 and into the catheter 60. In this latter embodiment, it may be desirable to include a component that facilitates attachment of the drug delivery catheter to the drug release device and/or stabilize such attachment, *e.g.*, substantially diminish movement of the drug delivery catheter in a direction perpendicular to the longitudinal axis of the drug release device (*e.g.*, to provide strain relief), so as to reduce risk of breakage of the drug delivery catheter at the attachment site.

The drug delivery catheter 60 comprises a lumen having a diameter that can be equal to, or can be greater or less than, the diameter of the drug release device orifice 73. Where the drug release system used in the drug delivery device dispenses drug by convection (as in, *e.g.*, osmotic drug delivery systems), the orifice size as well as the size of the lumen of the drug delivery catheter leading from the reservoir of the drug release system can be designed as described by Theeuwes (1975) *J. Pharm. Sci.* 64:1987-91. The orifice design criteria define the characteristics of the back-diffusion regulating element.

The drug delivery catheter 60 can have substantially the same inner and outer diameters throughout its length, or the inner diameter and/or outer diameter can vary along the catheter's length. Likewise, the walls of the drug delivery catheter can be of substantially the same thickness throughout its length, or can vary in thickness throughout the catheter's length. For example, the catheter can have an inner diameter that is equal to or greater than the diameter of the orifice at its proximal end, with a constriction smaller than the orifice of the release device at its distal end such that at least the inner diameter of the catheter tapers to a smaller drug delivery outlet at the distal end.

The drug delivery catheter 60 can comprise a catheter body 64 having any of a variety of dimensions and geometries, which are selected to be most suitable for the intended use of the drug delivery device (*e.g.*, the desired treatment site, the amount of drug to be delivered, the drug release device to be used in conjunction with the drug delivery catheter, the desired means of attachment of the catheter to the drug release device to facilitate flow of drug from the drug release device to the catheter, *etc.*). The catheter body 64 will typically have a length in the range from about 1 cm to 150 cm, usually having a length in the range from about 2-5 cm up to about 50 cm. The outside diameter of the catheter body will typically be in the range from about 0.1 mm (0.3 F) to 2 mm (6 F), usually being in the range from about 0.125 mm (0.4 F) to about 1 mm (3 F). In one embodiment, the drug delivery catheter has an outer diameter of about 0.009". The drug delivery catheter body will define an inner lumen typically having a diameter in the range from about 0.025 mm to 1.5 mm, usually being in the range from about 0.05 mm to 1 mm, with catheters having larger outside diameters usually having larger lumen diameters. In one embodiment, the drug delivery catheter has an inner diameter of about 0.009".

In general, the drug delivery catheter body has a length in the range from about 1 cm to about 200 cm, usually from about 15 cm to about 40 cm; an outside diameter in the range from about 0.125 mm (0.4 F) to about 3 mm, usually from about 0.66 mm (2 F) to about 0.5 mm; and an inside diameter in the range from about 0.05 mm to about 2 mm, usually from about

0.075 mm to about 0.5 mm (2 F). The outside diameter of the drug delivery catheter is less than the inside diameter of a lumen of the guide body 20 that is to be used in conjunction with the drug delivery device. It should also be noted that the drug delivery orifice 73 may be provided in the drug release device distal end 72 as a distinct opening or as a series of openings, *e.g.*, as in the context of a rate-limiting membrane, which membrane defines a plurality of openings through which drug may flow from the drug reservoir 74. In either embodiment, the inner diameter of at least the proximal end 61 is of a size sufficient to provide a leak-resistant or leak-proof drug flow path from the reservoir 74 through the drug delivery catheter lumen.

The dimensions of the drug delivery device (*e.g.*, dimensions of the drug release device, drug delivery catheter, *etc.*) can vary according to a variety of factors such as the treatment site for drug delivery, the guide with which the drug delivery device is to be used, the desired drug delivery rate, the length of the course of treatment, *etc.*

The drug delivery catheter may be produced from any of a variety of suitable, substantially impermeable materials, and may be manufactured from the same or different material as the impermeable reservoir of the drug release device. Impermeable materials suitable for use in production of the controlled drug release device as described above are generally suitable for use in the production of the drug delivery catheter. The drug delivery catheter can generally be made from a relatively stiff catheter material, since the guide will provide protection of tissue during placement of the drug delivery device, and thus avoid substantial tissue damage and trauma to the patient. Exemplary materials from which the drug delivery catheter can be manufactured include, but are not necessarily limited to, polymers; metals; glasses; polyolefins (high density polyethylene (HDPE), low density polyethylene (LDPE), linear low density polyethylene (LLDPE), polypropylene (PP), and the like); nylons; polyethylene terephthalate; silicones; urethanes; liquid crystal polymers; PEBAX™; HYTREL™; TEFLON™; perfluoroethylene (PFE) perfluoroalkoxy resins (PFA); poly(methyl methacrylate) (PMMA); multilaminates of polymer, metals, and/or glass; nitinol; and the like. In one embodiment, the drug delivery catheter is manufactured from a nickel titanium alloy (NITINOL™).

The drug delivery catheter can comprise additional materials or agents (*e.g.*, coatings on the external or internal catheter body surface(s)) to facilitate placement of the drug delivery catheter within the guide and/or to provide other desirable characteristics to the catheter. For example, the drug delivery catheter can be coated with silver or otherwise coated or treated with antimicrobial agents, thus further reducing the risk of infection at the treatment site.

In general, the material of the drug delivery catheter is selected so as to provide the catheter with the desired degree of flexibility or stiffness. The flexible or stiff nature of the drug delivery catheter can be substantially the same throughout its length, or can vary over its length, *e.g.*, a distal portion of the catheter may be more flexible or more stiff relative to the proximal portion. In general, the drug delivery catheter body 64 is sufficiently flexible so that it can pass through any tortuous bends in the implanted guide 10, so as to facilitate movement of the catheter through the twists and turns that may be present in the access pathway to the treatment site. The drug delivery catheter body is preferably sufficiently stiff so as to allow for pushing of the catheter through the guide, particularly for pushing the drug delivery catheter through such tortuous bends in the guide. Alternatively or in addition, a support member (*e.g.*, a guide wire) may be provided, *e.g.*, around the outside of the catheter body, to facilitate pushing of the catheter through the guide. The use of such a support member can allow for use of less stiff materials for the drug delivery catheter body.

The distal end of the drug delivery catheter can be shaped so as to allow for smooth passage through the guide, particularly where the guide is in a tortuous bending configuration. For example, the distal end of the catheter can be provided as a rounded tip that allows for the catheter to move smoothly around a guide bend (*e.g.*, where a square-ended catheter tip might catch on the sidewalls of the guide, thus frustrating positioning of the drug delivery device).

A number of variations on this basic drug delivery catheter design are contemplated by the present invention. For example, the distal end of the drug delivery catheter may optionally end in a one-way valve such as a duck bill valve to prevent retrograde flow in the drug delivery catheter, with external pressure at that distal end. Alternatively or in addition, the distal end may comprise a porous plug that serves as a filter element preventing particulate matter (including bacteria) from exiting from the drug delivery catheter and into the treatment site. The drug delivery catheter can also be provided as a multi-lumen catheter, where at least one lumen serves as a drug delivery conduit. In the multi-lumen embodiment, one of the lumen can define a space through which a guide wire is threaded to facilitate positioning of the drug delivery device within a lumen of a guide. The drug delivery catheter may comprise a single drug outlet at the distal end for delivery of drug at or near a treatment site, or may comprise a plurality of such drug outlets (*e.g.*, in the form of side holes along a portion of the distal end of the catheter).

In use, the drug delivery catheter 60 is threaded into the guide so that the distal end 62 of the drug delivery catheter defining a drug delivery outlet is positioned for delivery of drug at a treatment site. In one embodiment, the drug delivery catheter 60 is primed with drug, *e.g.*, is

substantially pre-filled with drug. Priming of the drug delivery catheter reduces delivery start-up time, *i.e.*, time related to movement of the drug from the drug release device to the distal end of the drug delivery catheter. This feature is particularly advantageous where the drug release device of the drug delivery device releases drug at relatively low flow rates (*e.g.*, 0.4 $\mu\text{l/day}$). The drug
5 used to prime the drug delivery catheter may be the same drug that is delivered from the drug release device of the drug delivery device, or may be a different drug or different formulation of the drug, *e.g.*, the drug delivery catheter itself may provide for a component of the therapeutic regimen.

Sealing element

10 In one embodiment, the drug delivery device 50 comprises a sealing element 28 (see, *e.g.*, Fig. 28). In general, the sealing element 28 is positioned on the outer surface of the drug delivery device so, when positioned within a guide, backflow of bodily fluids from the target tissue 45 and/or drug delivered from the drug delivery device 50 into the guide lumen is substantially inhibited. The materials suitable for manufacture of the sealing element of the drug delivery
15 device are substantially the same as those suitable for manufacture of sealing elements used within a guide as described above.

The sealing element can be provided as a separate element that is attached to the drug delivery device outer wall (*e.g.*, an O-ring positioned around the outer wall of the drug delivery device), or may be a continuous extension of the material of the drug delivery device outer wall.

20 The drug delivery device can comprise a single sealing element or a plurality of sealing elements, and such sealing element(s) can be positioned along any portion of the drug delivery device. In one embodiment, at least one sealing element is positioned at a distal portion of the drug delivery device, *e.g.*, at or near the distal end of a drug delivery catheter of the drug delivery device. In addition to providing a liquid-proof seal, the sealing element(s) can also serve to stably position the
25 drug delivery device within the guide.

Leash embodiment

In one embodiment, the drug delivery device comprises a leash for retrieving the drug delivery device. In general, the leash comprises a proximal end and a distal end, where the distal end is attached to a portion of the drug delivery device 50. The proximal end of the leash is
30 retained at the implantation site or access site in the subject, and may be retained within a portion of the distal end of the guide. Drug delivery devices comprising such a leash can be positioned at any point within the lumen of the guide (*e.g.*, at a site any distance from an access or implantation

site at which the drug delivery device is initially introduced into the guide). In this latter embodiment, the drug delivery device can further optionally comprise a drug delivery catheter.

The leash can be made from any suitable material that is of sufficient strength to allow retrieval of the drug delivery device from within the guide lumen. Exemplary materials include multifilament strands (*e.g.*, nylon), metals (*e.g.*, stainless steel, nickel titanium, beryllium, copper, nickel, and alloys thereof), polymers, glasses, plastics, and other suitable materials, which typically can be selected from the same or similar materials described above for manufacture of the catheter. In one embodiment, the leash is sufficiently stiff to allow pushing and position of the drug delivery device at a selected position along the guide. The position of the drug delivery device along the guide may affect drug delivery rate. For example, in the case of a diffusional drug delivery system, a drug delivery pathway is defined by the distance from the drug delivery device to the treatment site. By selecting the drug delivery pathway length, the drug delivery rate can be modified according to Equation I above, where the length of the drug delivery pathway is L , and the guide inner diameter is A .

Drugs for delivery using the drug delivery device

Any of a wide variety of drugs can be delivered using the drug delivery system of the invention. Drugs suitable for delivery are generally provided as flowable formulations, and are generally provided as liquids or semisolids. The drugs may be anhydrous or aqueous solutions, suspensions or complexes, and may be formulated with pharmaceutically acceptable vehicles or carriers, as well as additional inert or active ingredients. The drugs of formulations suitable for delivery using the invention may be in various forms, such as uncharged molecules, components of molecular complexes or pharmacologically acceptable salts. Also, simple derivatives of the agents (such as prodrugs, ethers, esters, amides, etc.) that are easily hydrolyzed by body pH, enzymes, etc., can be employed. Preferably the agents are formulated so as to remain stable for long periods of storage on the shelf or under refrigeration, as well as for long periods stored in an implanted drug delivery system of the invention.

Of particular interest is the treatment of diseases or conditions that require long-term therapy, *e.g.*, chronic and/or persistent diseases or conditions for which therapy involves treatment over a period of several days (*e.g.*, about 3 days to 10 days), to several weeks (*e.g.*, about 3 or 4 weeks to 6 weeks), to several months or years, up to including the remaining lifetime of the subject. Subjects who are not presently suffering from a disease or condition, but who are susceptible to such may also benefit from prophylactic therapies using the devices and methods of the invention.

Use of Guide and Drug Delivery Device

The drug delivery device and guide of the invention can be used in a wide variety of subjects, including humans. The guide and delivery device can be implanted at any convenient site within the subject's body and oriented for delivery to any desired treatment site. Generally, at least
5 a portion of the proximal end of the guide is retained at an accessible, subcutaneous site, (*e.g.*, under the skin of the arm, shoulder, neck, back, or leg), or at a subcutaneous site within a body cavity (*e.g.*, within the mouth). The proximal end of the guide can be at a site close (*e.g.*, within a few centimeters, *e.g.*, within about 2 cm), or at a site relatively distant (*e.g.*, more than about 30 cm, generally greater than about 50 cm to 100 cm) from the treatment site, and thus from the
10 ultimate site of drug delivery. A single guide and/or drug delivery device, or two or more guides and/or drug delivery devices can be implanted in a subject during the course of a therapeutic program.

The guide is generally designed to remain implanted in the subject for an extended period, *e.g.*, from several days, to several weeks, months, or years, and can be designed to be substantially
15 permanently implanted in the subject (*e.g.*, for the subject's remaining lifespan). The drug delivery devices are generally designed to remain partially or substantially completely implanted, preferably substantially completely implanted, within the guide for a predetermined administration period, and are normally removed and replaced at the end of such administration period. However, the drug delivery devices can be designed to remain implanted within the guide for extended periods.

20 The devices of the present invention are preferably rendered sterile prior to use. This may be accomplished by separately sterilizing each component, *e.g.*, by gamma radiation, steam sterilization or sterile filtration, *etc.*, then aseptically assembling the final system. Alternatively, the devices may be assembled, then terminally sterilized using any appropriate method.

Implantation of the guide

25 Insertion of the guide and drug delivery device can be accomplished using methods and tools that are well known in the art. Insertion of the guide is accomplished in a manner similar to insertion of any of a variety of catheters, *e.g.*, under aseptic conditions with at least some local or general anesthesia administered to the subject. Where the guide comprises radiopaque material, insertion of the guide and/or guide body can be monitored by X-ray or other means of visualization
30 of the guide insertion process. The guide and delivery device can be positioned for drug delivery in the subject in separate steps, or in a single step as a complete drug delivery system. The guide and/or drug delivery device can optionally comprise one or more anchoring elements, *e.g.*, rings or ears (see, *e.g.*, Fig. 4), for retaining the guide and/or drug delivery device at a local site.

Guide and drug delivery device combinations to provide a drug delivery system

The present invention encompasses any of a variety of combinations of guides and drug delivery devices. The combination of the guide and drug delivery device can be varied according to a variety of factors such as the specific treatment site to which drug is to be delivered, the drug formulation to be delivered, *etc.* The ability to vary the characteristics of the guide material and the drug delivery device material, particularly the material of a drug delivery catheter used in connection with the drug delivery device, provides the clinician or other health professional with a wide variety of drug delivery systems that can be selected according to the needs of the patient.

In general, the system of the invention comprises a drug delivery device, wherein all or at least a portion of the drug delivery device is positioned within a guide so that a drug delivery pathway is defined from a reservoir of drug within the drug delivery device to the treatment site. In one embodiment of interest, the drug delivery device comprises a drug delivery catheter. In use, the catheter of the drug delivery device is inserted into the guide lumen, and all or at least a portion of the drug delivery device is stably positioned within the guide. In this embodiment, it is important that the drug delivery catheter and the guide are manufactured from, or comprise coatings of, materials that facilitate sliding of the outer wall of the drug delivery catheter within the lumen defined by the inner wall of the guide. For example, the guide inner wall and/or outer diameter of the drug delivery device (*e.g.*, the outer wall of a drug delivery catheter) comprises a fluorelated polymer (*e.g.*, teflon), an olefin (*e.g.*, HDPE), a silicon-based coating, a hydrophilic coating, PARYLENETM, *etc.*

Exemplary embodiments of such variations, and exemplary methods for their implantation, are described in more detail below.

Relatively flexible guide with a relatively stiff drug delivery catheter

In one embodiment, the guide comprises a relatively soft or flexible guide body. In one access system of interest, the relatively flexible guide is used with a drug delivery device having a drug delivery catheter comprising relatively stiffer materials. The relatively soft or flexible guide body in this embodiment is sufficiently flexible so that it is well-tolerated within the body, is not prone to breakage or leakage, and provides a protective function to the surrounding tissue during insertion of the relatively stiff drug delivery catheter.

Implanting relatively flexible guide

Implantation of a relatively soft guide can be accomplished according to any of a variety of strategies. For example, the access pathway may be defined using a tunneling device 85, such as a rigid or semi-rigid cannula or trocar (see, *e.g.*, Figs. 29 and 30). The tunneling device 85 can be

substantially straight throughout its length (as exemplified in Fig. 29, or such as a splittable needle), or may be shaped to provide for positioning of the guide so as to define a non-linear pathway (as exemplified in Fig. 30). The tunneling device can be used to bore through tissue to access a site of delivery (*e.g.*, an intrathecal space within the spine) so that the distal end of the tunneling device is positioned adjacent or within the desired treatment site. A proximal portion of the tunneling device is retained at a readily accessible site, *e.g.*, an external or subcutaneous site. The lumen of the tunneling device defines a conduit from the accessible site to the treatment site.

The flexible guide is positioned within the cannula lumen either during initial insertion of the cannula, or in a subsequent step in which the flexible guide is threaded through the cannula.

Where the guide is inserted into the tunneling device in a subsequent step, it may be desirable to deliver the guide through the tunneling device lumen using a wire, particularly where the guide is so flexible that the material of the guide body cannot be readily pushed through the tunneling device lumen. For example, a wire or stylet can be positioned within the guide lumen, and the wire and guide inserted into the tunneling device lumen as exemplified in Fig. 30.

In one embodiment, the guide is designed to facilitate easy withdrawal of the insertion cannula following implantation. For example, where the guide to be used comprises a guide chamber or other element positioned at the guide proximal end, the guide chamber or other element is provided as an attachable element. As exemplified in Figs. 37 and 38, where the guide 10 comprises a guide chamber 16 at the proximal end, the guide chamber 16 is attached to the guide proximal end by means of an attaching element 30. The attaching element 30 can be any suitable element for facilitating permanent or reversible connection between the guide body and the guide chamber. Exemplary attaching elements include, but are not necessarily limited to, a press-fit lock, a threaded element, a bayonet connector, luer lock, snap fit tab and recess, *etc.* In this embodiment, the guide 10 without the attached guide chamber 16 can be positioned within the lumen of cannula 85 during initial insertion of the cannula, or in a subsequent step in which the guide is threaded through the cannula. Once the guide is in place, the cannula can be withdrawn over the body of the guide 10, and the guide chamber 16 attached by means of the attaching element 30.

Alternatively implantation of a relatively flexible guide can be accomplished using a wire, stylet, or other reinforcing element that imparts substantial stiffness to the guide for insertion to the treatment site. The reinforcing element can be introduced into the guide lumen, and the guide and reinforcing element combination implanted into the subject to place the guide distal end at the treatment site. The reinforcing element can be then be withdrawn, leaving the guide in place.

The guide can be readily adapted for use with a reinforcing element. For example, the guide can comprise a reinforcing element channel 24 (see, e.g., Figs. 31 and 32). The reinforcing element channel 24 can be positioned adjacent all or a portion of the guide body. In the embodiment illustrated in Figs. 31 and 32, the guide and wire are provided as a monorail type system, where the guide rides over the reinforcing element (exemplified by wire 87).

In another embodiment, the reinforcing element channel 24 is adapted for use with a pushing element, such as a mandrel, to facilitate implantation. As exemplified in Figs. 39 and 40, the reinforcing element channel 24 is closed at the guide distal end 12. During implantation a mandrel 110 or other pushing element is inserted into the reinforcing element channel 24 to facilitate positioning of the guide distal end at a treatment site. Once the guide is in place, the mandrel 110 is removed. The empty reinforcing element channel 24 can then be filled, with a liquid, semi-solid, or solid material, which material preferably comprises an antimicrobial agent (e.g., a bacteriostatic and/or bactericidal agent). In addition, or alternatively, the inner wall of the reinforcing element channel is coated with antimicrobial coating. The drug delivery device 50 can be positioned within the guide lumen 13 during implantation, or inserted into the guide lumen 13 following implantation (e.g., before or after withdrawal of the mandrel). In one embodiment, the drug delivery device is stably positioned within the guide through a stable positioning element (e.g., a locking/docking mechanism) that utilizes a portion of the reinforcing element channel 24.

The guide can be relatively flexible throughout its length, or may be relatively flexible for only a portion of its length, e.g., relatively flexible over a distal portion of the guide body. Where the guide is flexible only over a portion of its length and comprises a reinforcement channel, the reinforcement element channel can be positioned adjacent only the relatively flexible portion of the guide.

Positioning of relatively stiff catheter in relatively flexible guide

Drug delivery catheters that are relatively stiff can be readily pushed through the relatively flexible guide, providing for ease in insertion of the catheter into the guide and placement at the treatment site. The use of the relatively flexible guide with a relatively stiff drug delivery catheter is advantageous in that the guide serves to protect the surrounding tissue from the drug delivery catheter. In this embodiment it may be desirable for the distal end of the drug delivery catheter to be blunt, rounded, or tapered to avoid catching of the drug delivery catheter end against an inner wall of the guide and/or to prevent damage to the tissue at or surrounding the treatment site.

Relatively stiff guide with relatively flexible drug delivery catheter

Alternatively, it may be desirable to use a guide having a relatively stiff guide body with a drug delivery device having a relatively soft or flexible drug delivery catheter. If a guide body is of sufficient stiffness, the guide can be implanted within the subject without the use of, for example, a tunneling device or reinforcement element. Where the guide is relatively stiff, the drug delivery catheter can be relatively more flexible throughout its length or, for example, at a distal portion of the catheter. The flexible drug delivery catheter may be of particular use where it is desirable to deliver drug from the catheter at a point distally beyond the distal end of the guide.

Placement of drug delivery device

Once the guide is in place, then the drug delivery device is positioned within the guide to facilitate delivery of drug from the drug delivery device and to the treatment site. In general, the drug delivery device is placed in the guide by inserting the drug delivery device distal end into the guide lumen to position the drug delivery device for delivery of drug from the device's drug reservoir to the treatment site.

Where the drug delivery device comprises a drug delivery catheter, the catheter can be inserted into the guide lumen and up to and/or through the guide distal end. The drug release device is then positioned at or within the guide proximal end, and may be retained thereat or therein via any of a variety of stable positioning elements as described above. The guide proximal end and the drug release device retained therein are generally retained at a subcutaneous site as described above.

Re-access of the treatment site

The guide provides for ready access and re-access to the treatment site, thus providing a conduit for drug delivery, sampling, *etc.* For example, where the guide is used in conjunction with a drug delivery device, the drug delivery device can be readily positioned within the guide to facilitate delivery of the drug to the treatment site. When desirable, the drug delivery device can be easily removed, and, where desirable, replaced with a new drug delivery device.

Removal and/or replacement of the drug delivery device can be accomplished using tools and methods that are readily available. For example, where a proximal portion of the drug delivery device and/or guide is retained at a subcutaneous site, the drug delivery device can be removed by first locating the guide proximal end (and/or drug release device proximal end) by fingertip palpation of the subcutaneous site of insertion. After anesthetizing the subject at least locally, an incision is made through the skin and any fibrous capsule tissue surrounding the area of implantation. The end of the device opposite the incision is pushed so that the proximal end of the

guide is urged out of the incision. The drug delivery device can then be released from the guide and withdrawn. A replacement drug delivery device, which device may comprise the same or different drug and drug formulation, can then be inserted into the guide as described above. Upon placement of the drug delivery device and securing of the device in the guide, the guide is then
5 urged back into the original incision, and the incision closed. This procedure can be designed so that removal and replacement of drug delivery devices can be performed on an outpatient basis, and with minimal discomfort to the subject.

EXAMPLES

10 The following examples are put forth so as to provide those of ordinary skill in the art with a complete disclosure and description of how to make and use various constructs and perform the various methods of the present invention and are not intended to limit the scope of what the inventors regard as their invention nor are they intended to represent or imply that the embodiments described below are all on the only embodiments constructed or tested. Efforts have
15 been made to ensure accuracy with respect to numbers used (e.g., amounts, concentrations, particular components, etc.) But some deviations should be accounted for.

Example 1

In one embodiment, the guide is a composite of teflon on the inside diameter of the guide
20 and silicone laminated on the outside, and has an outer diameter of about 0.040" and an inner lumen diameter of about 0.012". The proximal end of the guide is adapted to receive the distal portion of a drug release portion of a drug delivery device, and includes titanium guide chamber that houses the drug delivery device. The guide is flexible, and is implanted into the subject using a rigid or semi-rigid cannula.

25

Example 2

In one embodiment, the drug delivery device is an implantable osmotic pump (e.g., DUROS™) having a drug delivery catheter attached to the a distal portion of the pump so as to provide a drug delivery pathway from the reservoir of the pump and through the catheter. The
30 drug delivery catheter is made from a nickel titanium alloy, and has an inner diameter of about 0.006", and an outer diameter of about 0.010".

The invention as shown and described is considered to be the one of the most practical and preferred embodiments. It is recognized, however, that the departures may be made therefrom which are within the scope of the invention and that obvious modifications will occur to one skilled in the art upon reading this disclosure.

WHAT IS CLAIMED IS:

1. An implantable guide for facilitating repeated access to a treatment site in a subject, the guide comprising:
 - 5 a proximal end, a distal end, and a guide body, wherein the guide body defines a lumen extending from the guide proximal end to the guide distal end; and
 - a stable positioning element for stably positioning at least a portion of a drug delivery device within the guide.
- 10 2. The implantable guide of claim 1, where at least a portion of the guide body is flexible.
3. The implantable guide of claim 1, wherein the guide comprises an openable valve.
4. The implantable guide of claim 1, wherein the guide comprises a sealing element
15 positioned within the guide lumen.
5. The implantable guide of claim 1, wherein the guide body defines a plurality of lumen.
6. The implantable guide of claim 1, wherein the guide is adapted to accommodate at least
20 two drug delivery devices.
7. The implantable guide of claim 1, wherein the guide further comprises a reinforcing element channel.
- 25 8. The implantable guide of claim 1, wherein the guide further comprises an anchoring element.
9. The implantable guide of claim 1, wherein the guide body comprises a material selected
30 from the group consisting of: a polymer, a metal, glass, a polyolefin, nylon, polyethylene terephthalate, silicon, urethane; a liquid crystal polymer and a fluorelated polymer.

10. The implantable guide of claim 1, wherein the guide is shaped for implantation to a treatment to a site that is subcutaneous, intravenous, intrathecal, intraorbital, intraocular, intraaural, intratympanic, intramuscular, intra-arterial, intra-articular, intracavitary, intraductal, intraglandular, intravascular, intranasal, intraperitoneal, intraspinal, epidural, intracranial, intracardial,
5 intrapericardial, peritumoral, or intratumoral.

11. An implantable guide for facilitating repeated access to a treatment site in a subject, the guide comprising:

a proximal end, a distal end, and a guide body, wherein the guide body defines a lumen
10 extending from the guide proximal end to the guide distal end; and
a sealing element for providing a liquid-resistant seal with at least a portion of a drug delivery device positioned within the guide lumen.

12. The implantable guide of claim 11, wherein at least a portion of the guide body is
15 flexible.

13. The implantable guide of claim 11, wherein the guide comprises an openable valve.

14. The implantable guide of claim 11, wherein the guide comprises a stable positioning
20 element for stably positioning at least a portion of a drug delivery device within the guide.

15. The implantable guide of claim 11, wherein the guide body defines a plurality of lumen.

25 16. The implantable guide of claim 11, wherein the guide is adapted to accommodate at least two drug delivery devices.

17. The implantable guide of claim 11, wherein the guide further comprises a reinforcing element channel.
30

18. The implantable guide of claim 11, wherein the guide further comprises an anchoring element.

19. The implantable guide of claim 11, wherein the guide body comprises a material selected from the group consisting of: a polymer, a metal, glass, a polyolefin, nylon, polyethylene terephthalate, silicon, urethane; a liquid crystal polymer and a fluorelated polymer.

5 20. The implantable guide of claim 11, wherein the guide is shaped for implantation to a treatment to a site that is subcutaneous, intravenous, intrathecal, intraorbital, intraocular, intraaural, intratympanic, intramuscular, intra-arterial, intra-articular, intracavitary, intraductal, intraglandular, intravascular, intranasal, intraperitoneal, intraspinal, epidural, intracranial, intracardial, intrapericardial, peritumoral, or intratumoral.

10

21. A drug delivery device comprising:

a drug release device comprising a reservoir, and an orifice defined by a distal portion of the drug release device;

15 a substantially hollow drug delivery catheter comprising a drug delivery catheter proximal end and a drug delivery catheter distal end, wherein the drug delivery catheter proximal end is coupled to the drug release device to provide a drug flow pathway from the reservoir, through the orifice, and through a lumen of the drug delivery catheter; and

a stable positioning element for stably positioning at least a portion of the drug delivery device within a guide.

20

22. The drug delivery device of claim 21, wherein the stable positioning element comprises a recess for receiving a snap fit tab.

23. The drug delivery device of claim 21, wherein the drug delivery device further
25 comprises a sealing element for providing a liquid-resistant seal with a guide.

24. The drug delivery device of claim 21, wherein the drug delivery catheter comprises a material selected from the group consisting of: a polymer, a metal, glass, a polyolefin, nylon; polyethylene terephthalate, silicone, urethane, a liquid crystal polymer, a fluorelated polymer, and
30 nitinol.

25. The drug delivery device of claim 21, wherein the drug delivery catheter comprises nitinol.

26. The drug delivery device of claim 21, wherein the drug delivery catheter is coated with silver or an antimicrobial agent.

27. A drug delivery device comprising:

5 a drug release device comprising a reservoir, and an orifice defined by a distal portion of the drug release device;

a substantially hollow drug delivery catheter comprising a drug delivery catheter proximal end and a drug delivery catheter distal end, wherein the drug delivery catheter proximal end is coupled to the drug release device to provide a drug flow pathway from the reservoir, through the orifice, and through a lumen of the drug delivery catheter; and

10 a sealing element for providing a liquid-resistant seal with a guide.

28. The drug delivery device of claim 27, wherein the drug delivery device comprises a stable positioning element for stably positioning at least a portion of the drug delivery device within a guide.

29. The drug delivery device of claim 27, wherein the stable positioning element is a snap fit recess for mating with a snap fit tab.

20 30. The drug delivery device of claim 27, wherein the drug delivery catheter comprises a material selected from the group consisting of: a polymer, a metal, glass, a polyolefin, nylon, polyethylene terephthalate, silicone, urethane, a liquid crystal polymer, a fluorelated polymer, and nitinol.

25 31. The drug delivery device of claim 27, wherein the drug delivery catheter comprises nitinol.

32. The drug delivery device of claim 27, wherein the drug delivery catheter is coated with silver or an antimicrobial agent.

30

33. A system for delivery of drug to a treatment site comprising:
an implantable guide comprising a proximal end, a distal end, and a guide body, wherein the guide body defines a lumen extending from the guide proximal end to the guide distal end;
a drug delivery device, wherein at least a portion of the drug delivery device is removably
5 and stably positioned within the guide lumen; and
a stable positioning element that stably and removably associates the guide with the drug delivery device;
wherein the drug delivery device is positioned for delivery of drug from a drug reservoir of the drug delivery device and through the distal end of the guide lumen to the treatment site.
- 10 34. The system of claim 33, wherein the drug delivery device comprises:
a drug release device comprising a drug reservoir and a distal portion defining a drug delivery orifice; and
a drug delivery catheter comprising a drug delivery catheter proximal end and a drug
15 delivery catheter distal end, wherein the drug delivery catheter proximal end is coupled to the drug release device to provide a drug delivery pathway from the drug reservoir, through the orifice, and through a lumen of the drug delivery catheter to the drug delivery catheter distal end.
- 20 35. The system of claim 34, wherein the drug release device is selected from the group consisting of a diffusion system, an osmotic pump, an electromechanical pump, an erodible drug-comprising polymer, an electrodiffusion pump, an electroosmotic pump, a piezoelectric pump, a vapor pressure pump, and an electrolytic pump.
- 25 36. The system of claim 34, wherein the drug delivery catheter distal end terminates within the guide body.
37. The system of claim 34, wherein the drug delivery catheter distal end terminates at a point distal to the guide distal end.
- 30 38. The system of claim 34, wherein the drug delivery catheter is at least partially filled with drug prior to implantation.

39. The system of claim 33, wherein the guide comprises an outer diameter of from about 0.1 mm to 3 mm.

40. The system of claim 34, wherein the drug delivery catheter comprises an inner
5 diameter of from about 0.025 mm to 1.5 mm.

41. The system of claim 34, wherein the drug delivery catheter is stiff relative to the guide body of the guide.

10 42. The system of claim 33, wherein at least a portion of the guide body is flexible.

43. A system for delivery of drug to a treatment site comprising:
an implantable guide comprising a proximal end, a distal end, and a guide body, wherein
the guide body defines a lumen extending from the guide proximal end to the guide distal end;
15 a drug delivery device, wherein at least a portion of the drug delivery device is removably
and stably positioned within the guide lumen; and
a sealing element positioned between an inner wall of the guide lumen and an outer wall of
the drug delivery device;
wherein the drug delivery device is positioned for delivery of drug from a drug reservoir of
20 the drug delivery device and through the distal end of the guide lumen.

44. The system of claim 43, wherein the system further comprises a stable positioning
element for associating the drug delivery device with the guide.

25 45. The system of claim 43, wherein the stable positioning element comprises a snap fit
tab.

46. The system of claim 43, wherein the stable positioning element comprises a bayonet-
style connector.

30 47. The system of claim 43, wherein the stable positioning element comprises a luer lock.

48. The system of claim 43, wherein the stable positioning element comprises a threaded coupling member.

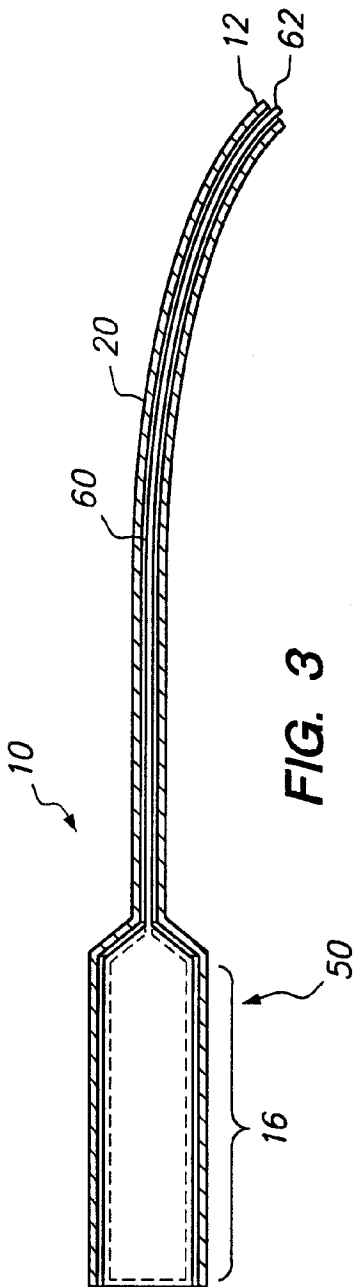
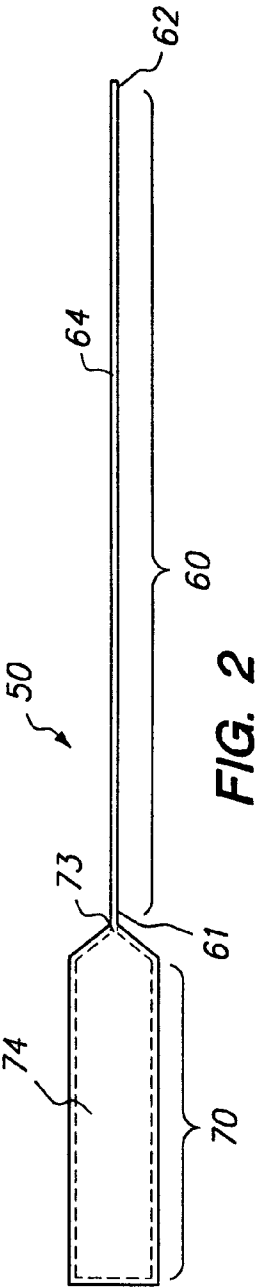
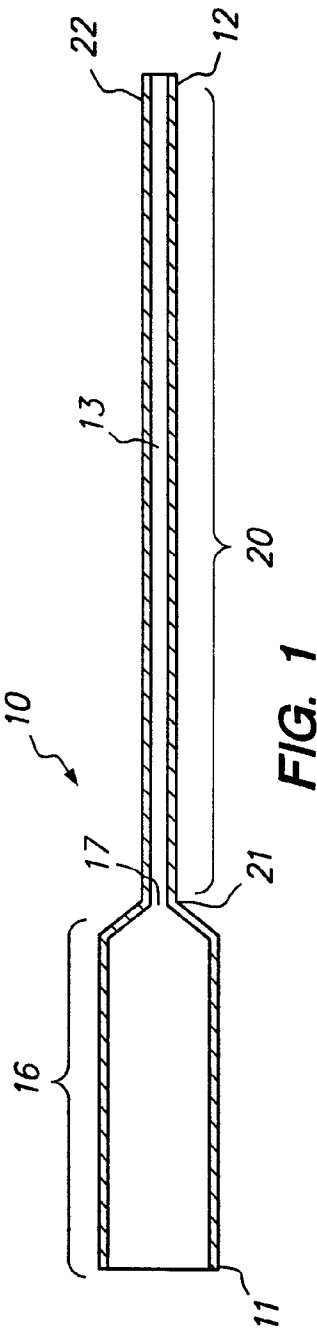
5 49. The system of claim 43, wherein the stable positioning element comprises a press-fit connection.

50. A method for site-specific drug delivery, the method comprising:
implanting in a subject a guide of claim 1, said implanting providing for placement of the guide distal end at a treatment site;
10 inserting at least a portion of a drug delivery device into the implanted guide, said insertion providing for stable positioning of the drug delivery device at a proximal end of the guide; and
delivering a drug from the drug delivery device to the treatment site from the guide distal end.

15 51. The method of claim 50, wherein the drug delivery device comprises a drug release device and a drug delivery catheter, and wherein the drug release device is retained at the proximal end of the guide and the drug delivery catheter is positioned within the guide lumen.

20 52. The method of claim 50, wherein the treatment site is subcutaneous, intravenous, intrathecal, intraorbital, intraocular, intraaural, intratympanic, intramuscular, intra-arterial, intra-articular, intracavitary, intraductal, intraglandular, intravascular, intranasal, intraperitoneal, intraspinal, epidural, intracranial, intracardial, intrapericardial, peritumoral, or intratumoral.

25 53. A method of providing access to a treatment site, the method comprising:
implanting in a subject a guide of claim 1, said implanting providing for placement of the guide distal end at a treatment site;
wherein the guide defines a conduit for access to the treatment site.



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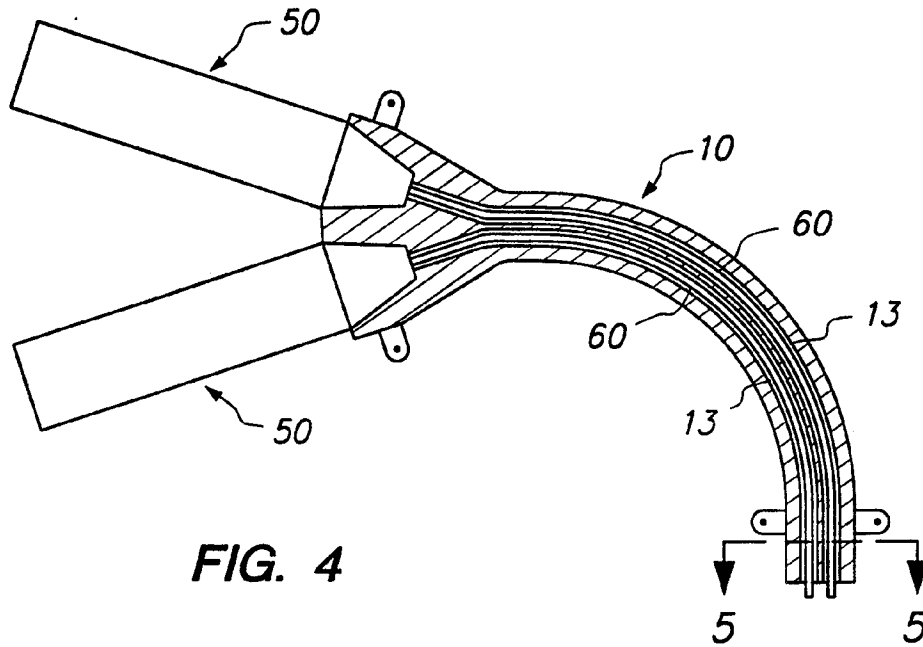


FIG. 4

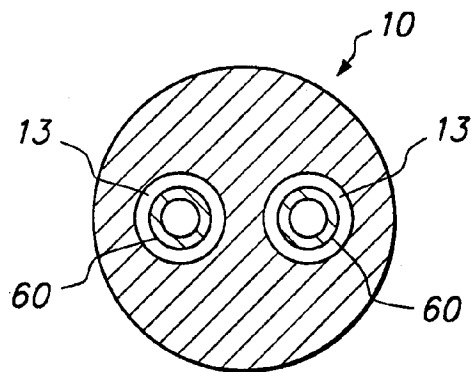


FIG. 5

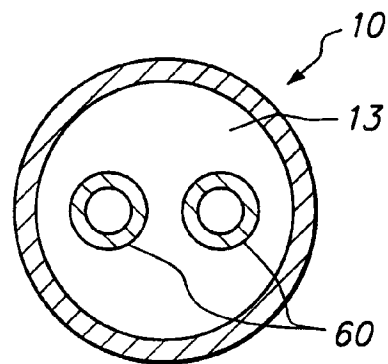
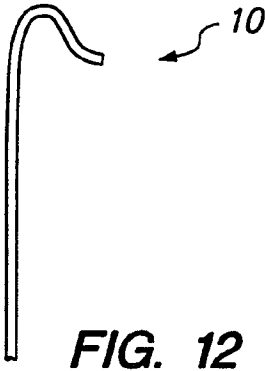
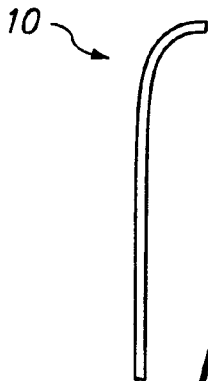
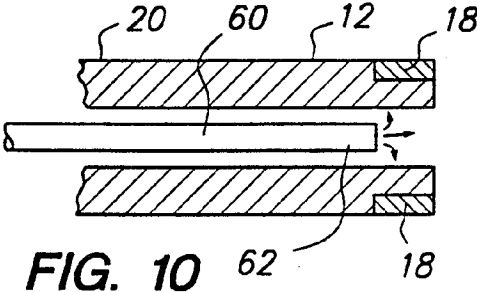
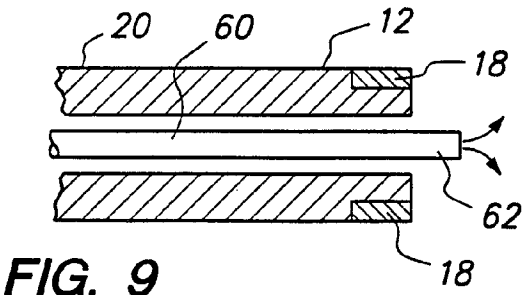
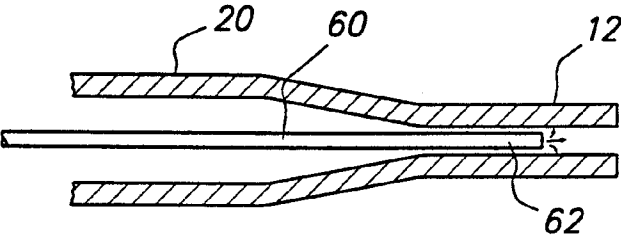
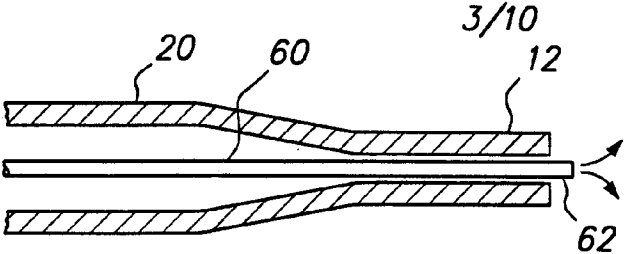


FIG. 6



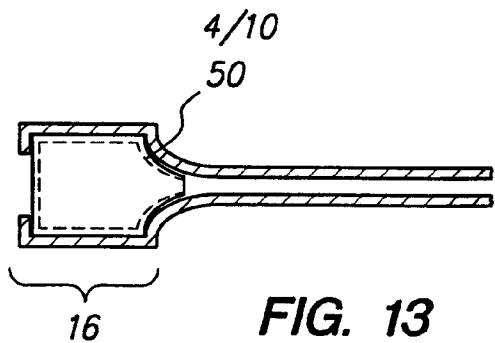


FIG. 13

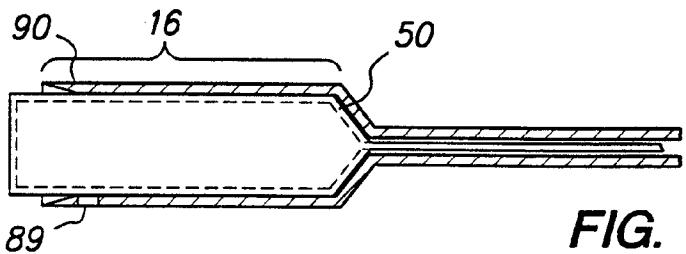


FIG. 14

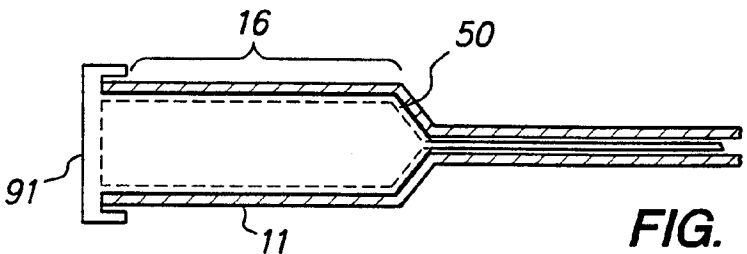


FIG. 15

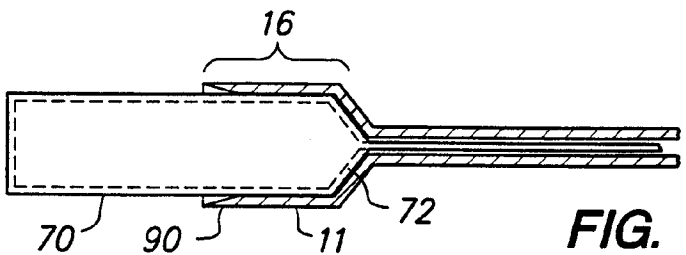


FIG. 16

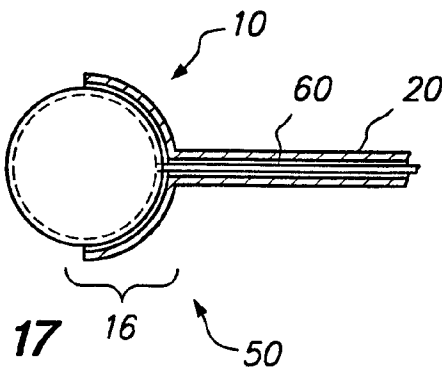


FIG. 17

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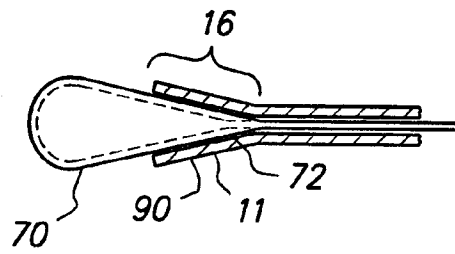


FIG. 18

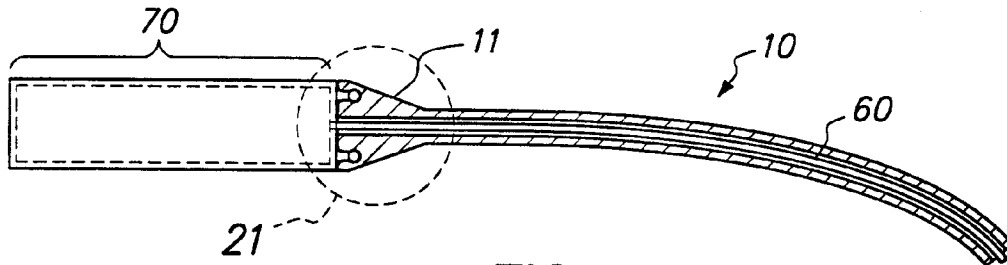


FIG. 19

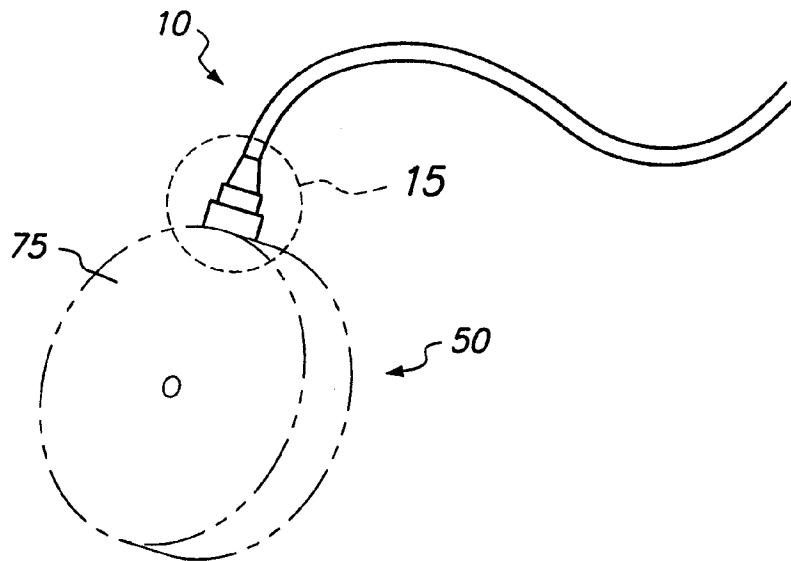


FIG. 20

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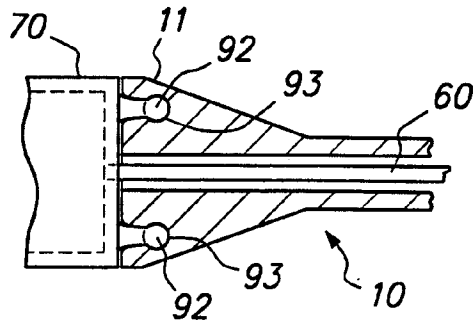


FIG. 21

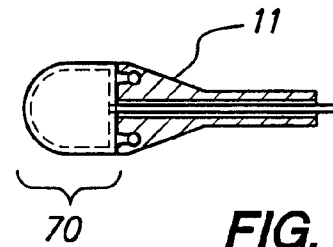


FIG. 22

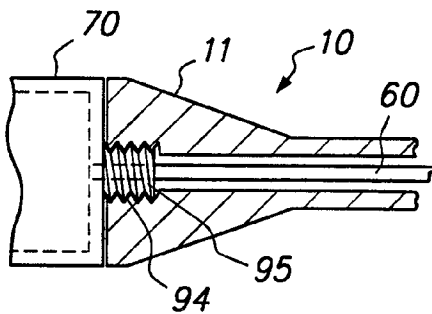


FIG. 23

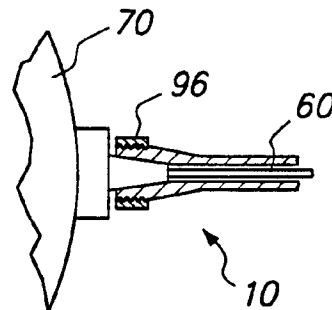


FIG. 24

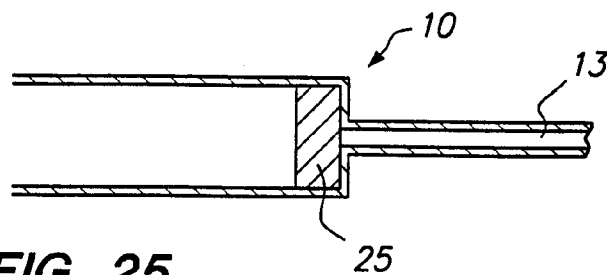


FIG. 25

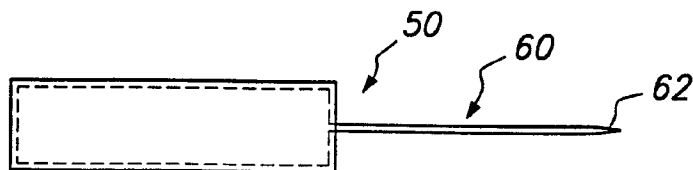


FIG. 26

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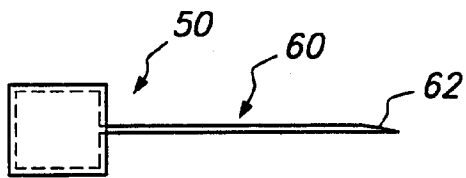


FIG. 27

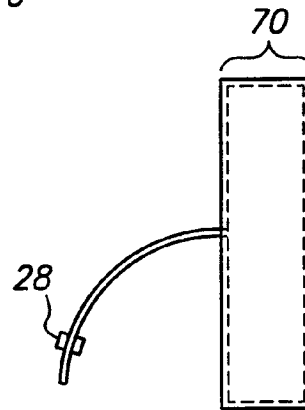


FIG. 28

FIG. 29

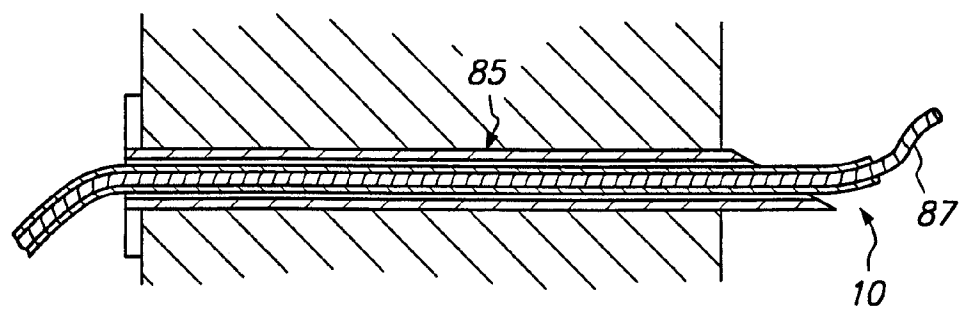
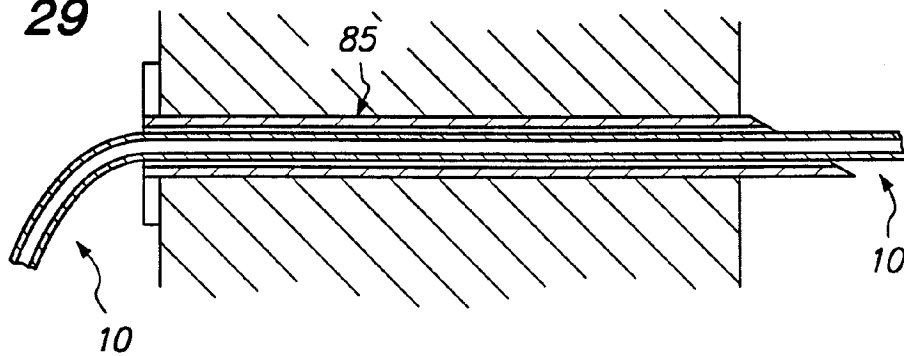


FIG. 30

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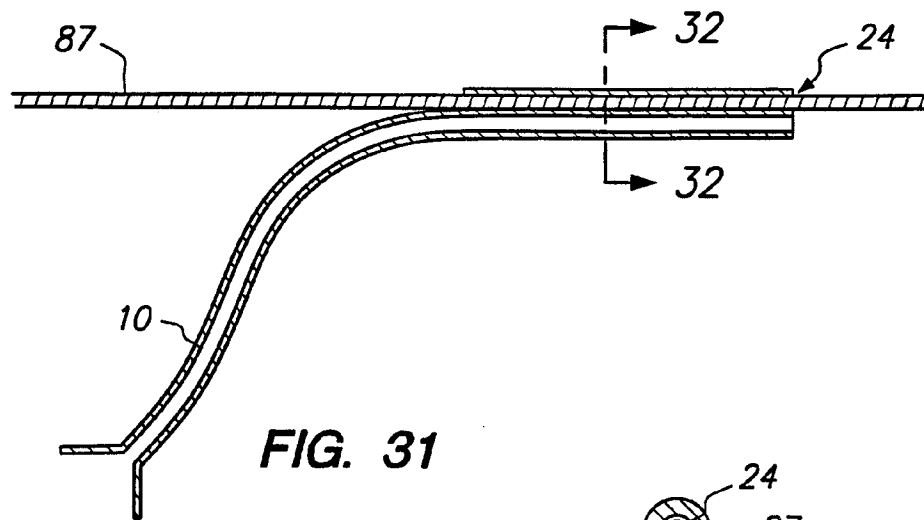


FIG. 31

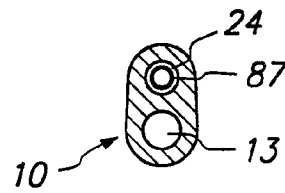


FIG. 32

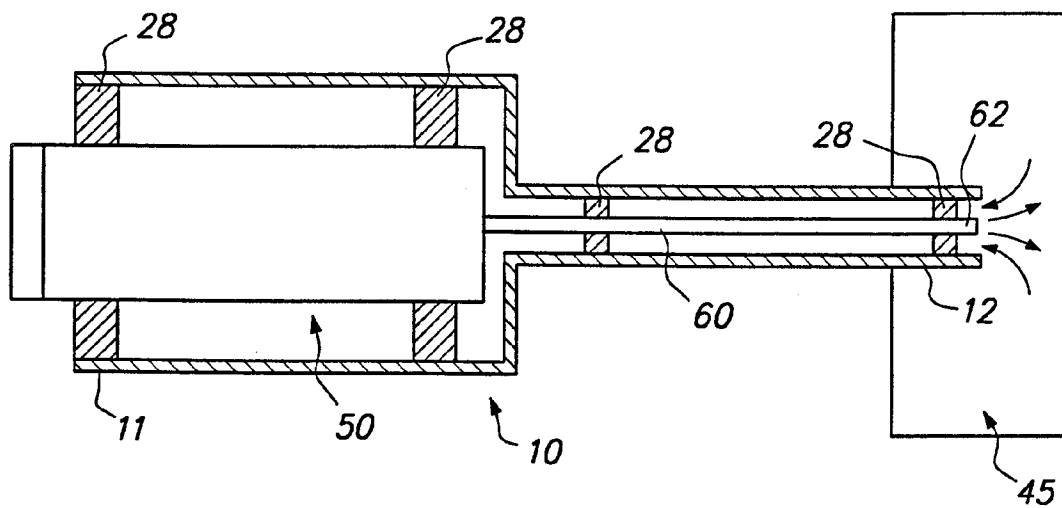
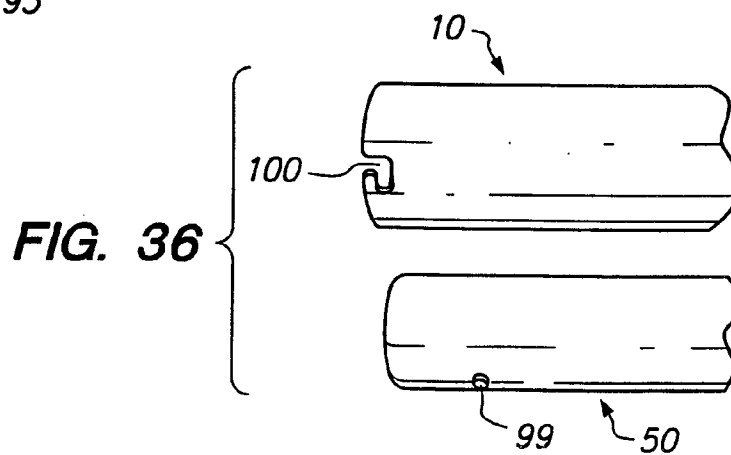
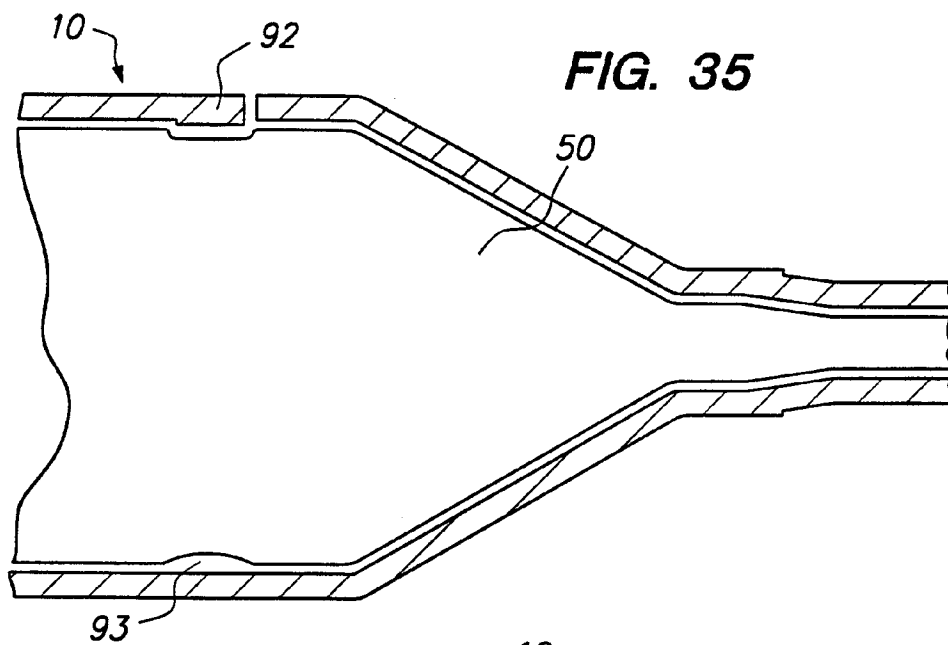
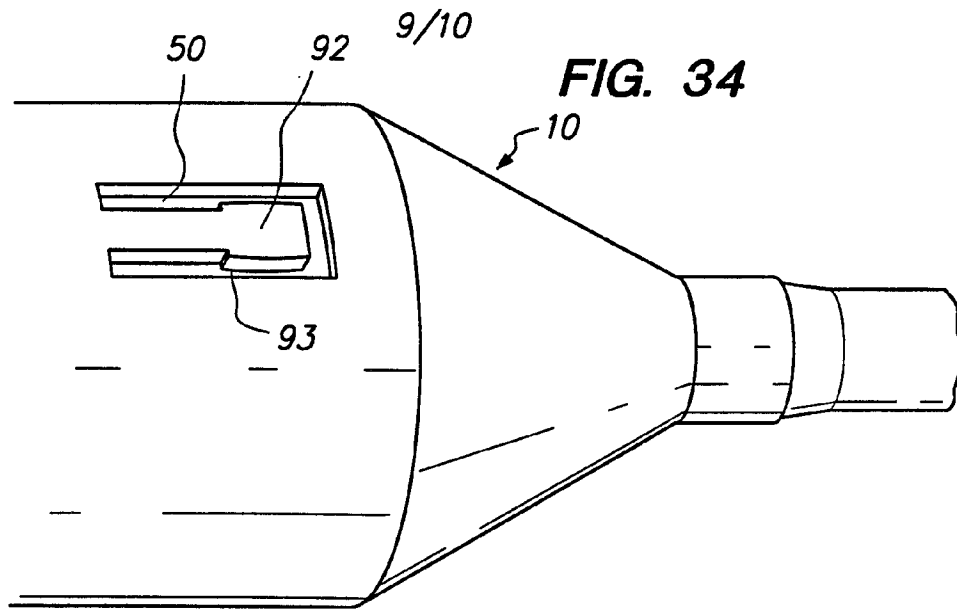
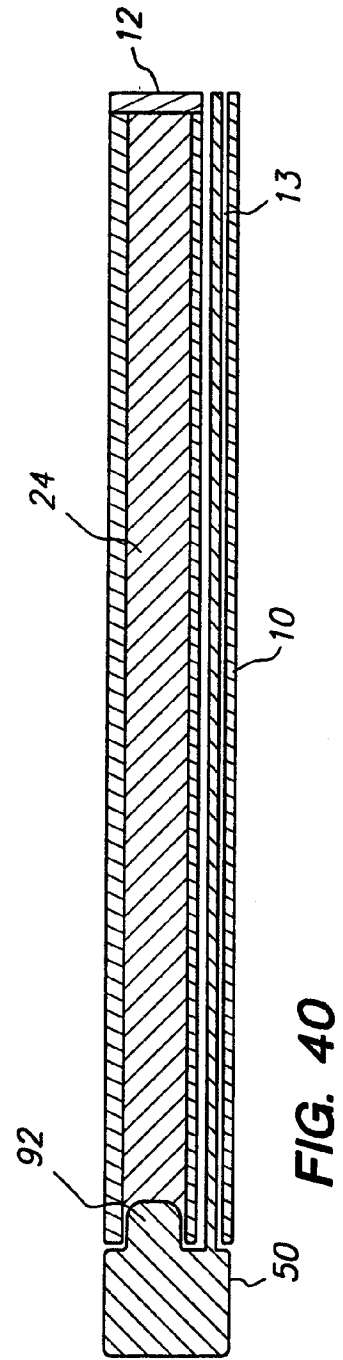
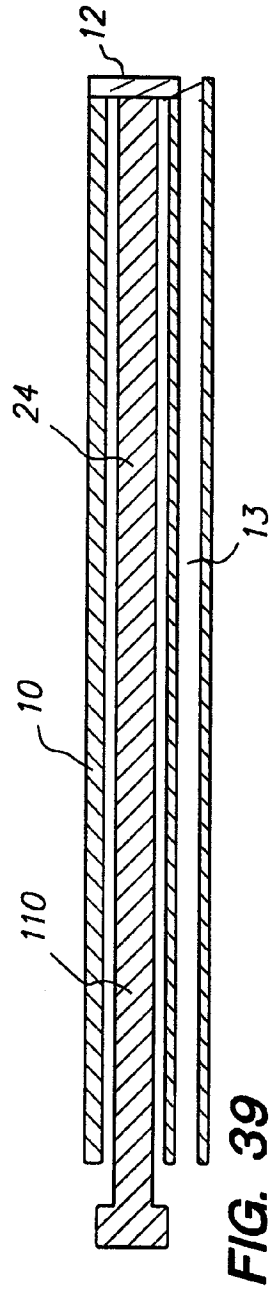
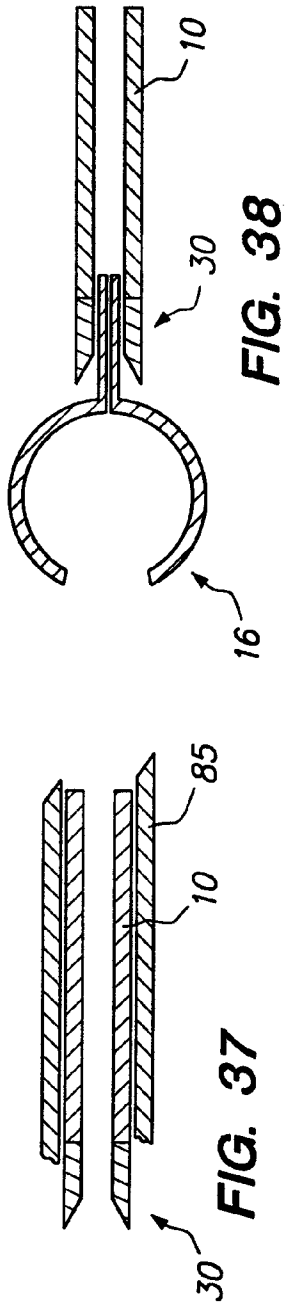


FIG. 33



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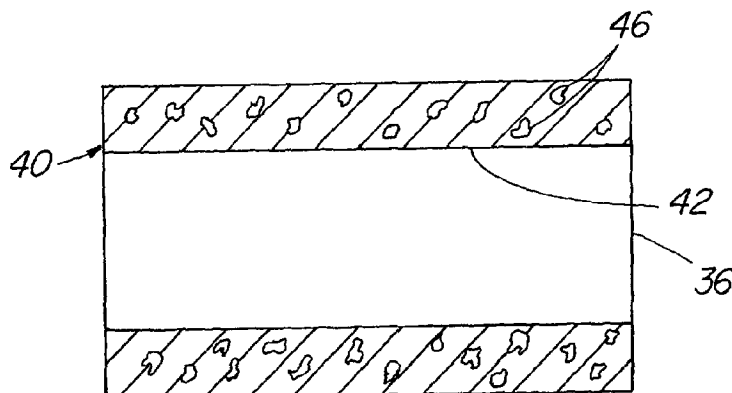
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(54) Title: INTRODUCER SHEATH



(57) Abstract: An introducer sheath (30) having a short distal tip section (34, 40) that is highly radiopaque. The distal tip section may be of FEP with 20 % to 75 % by weight tungsten particulate filler, and may be initially a separate member (40) and bonded to the sheath shaft distal end (32).

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INTRODUCER SHEATH

Description

Technical Field

The present invention relates generally to the field of medical devices and more particularly to introducer sheaths.

Background of the Invention

5 An introducer sheath is utilized in the percutaneous placement of a guide wire or catheter into a blood vessel, and comprises a flexible tube that itself is introduced into the blood vessel over a dilator. Once in position, the dilator is removed from within the sheath and withdrawn from the patient, and the guide wire or catheter is inserted through the sheath into the patient. Such sheaths are of biocompatible polymeric material and preferably contain an amount of radiopaque material in the polymeric matrix, and include a short tapered distal tip portion. Sheaths should have sufficient radial rigidity to remain open or patent upon removal of the dilator, but be sufficiently flexible to permit manipulation without kinking, under conditions of normal use. Internal sheath diameters range from 4 French to 10 26 French (1.3 mm to 8.7 mm) to accommodate the outside diameters of dilators and catheters and wire guides to extend therethrough.

15 Introducer sheaths are known that include adjacent to the distal tip portion, a radiopaque marking distinct from the remainder of the sheath, to indicate through fluoroscopy the position of the distal tip portion of the sheath within the patient, to assure proper positioning. The sheath can be of fluorinated ethylene propylene (FEP) having about 5 to 40% by weight loading of barium filler. Introducer sheaths have been known that include an annular ring of radiopaque paint on the sheath adjacent to the distal tip. Also, such marking typically can be an annular band of platinum alloy, or tungsten or gold or the like that is secured within the outer surface of the sheath adjacent to the distal tip, as in the CHECK-FLO PERFORMER Introducer Sheath sold by Cook Incorporated, Bloomington, IN. The metal band is spaced 25 approximately one-quarter inch from the distal tip and imparts substantial rigidity to

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the somewhat flexible sheath, whereas it would be desirable for the sheath to flex sufficiently during positioning to temporarily assume an oval cross-section locally.

It has been known to provide catheters such as introducer catheters with elongate flexible soft distal tip portions to minimize vessel wall trauma. It has been known to provide such distal tip portions as initially separate members that are bonded to the distal end of the catheter tube, with the tip member having filler material therein for viewing by fluoroscopy. The catheter shaft may be of a multiple layer construction using different materials and may include a wire coil to maintain lumen patency. Catheter constructions utilizing initially separate distal tip members bonded to a shaft, are disclosed in U.S. Patents Nos. 4,898,591; 5,045,072; 5,300,048; 5,584,821; and 5,769,830. However, such tip members are commonly made of copolymers that can be substantially loaded such as by tungsten, barium or bismuth, while the remainder of the catheter shaft contains substantially less radiopaque material adjacent to the distal tip portion.

It is desired to provide an introducer sheath in which the radiopaque marking is exactly at the distal tip rather than spaced slightly proximally from the tip, to best assure exact positioning by the surgeon.

Summary of the Invention

The foregoing problems are solved and a technical advance is achieved in an illustrative introducer sheath that includes a short distal tip section that is substantially more radiopaque than the radiopaque material of the remainder of the polymeric sheath shaft proximally from the distal tip. The distal tip may be a short initially separate ring of polymeric material affixed onto the distal end of the sheath shaft to define the distal tip section. The ring is made preferably of fluorinated ethylene propylene (FEP) containing a filler of tungsten or similar metal particles between about 20 to 75% by weight, while the sheath shaft is also of FEP with a substantially lower radiopaque filler content.

The present invention also is directed to a radiopaque composition of fluorinated ethylene propylene containing a loading of between about 20% to about 75% radiopaque filler, thereby being highly radiopaque, with the filler being tungsten, tantalum, platinum, gold, or lead or other metal.

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Brief Description of the Drawings

An embodiment of the introducer sheath of the present invention will now be described by way of example with reference to the accompanying drawings.

FIGURE 1 is an illustration of a Prior Art introducer sheath containing a metal radiopaque band proximate the distal tip;

FIGURE 2 is an enlarged partial cross-section view of the distal tip region of an introducer sheath containing the present invention; and

FIGURE 3 shows an initially separate tip member with filler.

Detailed Description

FIG. 1 illustrates an introducer sheath 10 of the prior art, having a shaft 12 having a distal tip 14 and a proximal end 16, and through which extends a lumen. Shaft 12 is polymeric, such as of fluorinated ethylene propylene and contains a radiopaque filler such as an 8 to 12% loading of barium sulphate. Adjacent to the distal end 14 is an annular band 18 of platinum alloy or gold that is highly radiopaque. Distal tip 14 has a tapered outer surface 20 to facilitate insertion into a patient, and metal band 18 embedded within the wall of sheath 10 and is spaced from distal tip 14 about one-quarter inch to assure against becoming dislodged during insertion and removal of the sheath from a patient. During use, a surgeon must estimate the exact location of distal tip 14 distally of the metal band 18, as discerned through fluoroscopy.

FIG. 2 illustrates the distal sheath portion containing the radiopaque distal tip section of the present invention. Sheath shaft 30 includes an end 32, with distal tip section 34 extending distally therefrom to a leading distal end 36 and having a tapered outer surface 38 thereat. Distal tip section 34 may be initially fabricated as a separate member 40 having a lumen 42 equal in diameter of lumen 44 of shaft 30, of a polymeric material that is at least similar enough to the polymeric material of the shaft to be easily and successfully bonded thereto. Such a member is easily extruded and cut to a short length, as shown in FIG. 3.

As an example, member 40 is extruded preferably from fluorinated ethylene propylene having dispersed therein a filler of tungsten particles 46 between about 20% and about 75% by weight, such as preferably about 50 to 55% by

- 4 -

weight. The tungsten particles preferably range in size from about 0.5 microns to 25 microns, and more preferably are about 1.4 microns to about 1.8 microns in size. Other polymeric materials include nylon, polyethylene, polyurethane and polytetrafluoroethylene, and other radiopaque filler materials include tantalum, titanium, platinum, gold, silver, bismuth trioxide and lead and the like. It is unexpected that such high loading could be attained with FEP and still result in a stable extrudable composition that can be bonded at least to other FEP material. A loading of 20% tungsten results in a radiopacity that is roughly equivalent to that generated by a 40% loading of barium sulphate.

FEP sheaths have heretofore contained about 5 to 40% barium sulphate filler. Fluorinated ethylene propylene is not known to be fillable to over 40% with barium sulphate particles and still result in a stable extrudable composition. Generally, the particles of barium sulphate used in current introducer sheaths are between about 0.7 microns and 10 microns, preferably about 1 to 3 microns in size. It is believed that an irregular, nonspherical shape of metal particles, along with the high density of the metal, small particle size and narrow size distribution range, may permit such high loading levels in the present invention.

Member 40 can be cut to a length of for example one-quarter inch and be bonded onto an end of shaft 30 such as by adhesive or by thermal bonding, and thereafter be machined for finishing. One such thermal bonding method is disclosed in U.S. Patent No. 5,017,259 for use with catheters. In accordance with U.S. Patent No. 5,769,830, a thermal bond is attained by inserting a mandrel through the tubular shaft and the tip member and then inserted into a forming die to which radiofrequency energy is commonly applied for melting together the materials of the distal end portion of the sheath and the distal tip member.

- 5 -

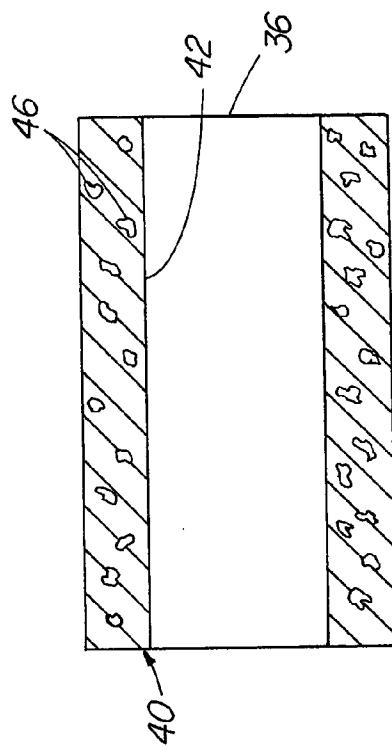
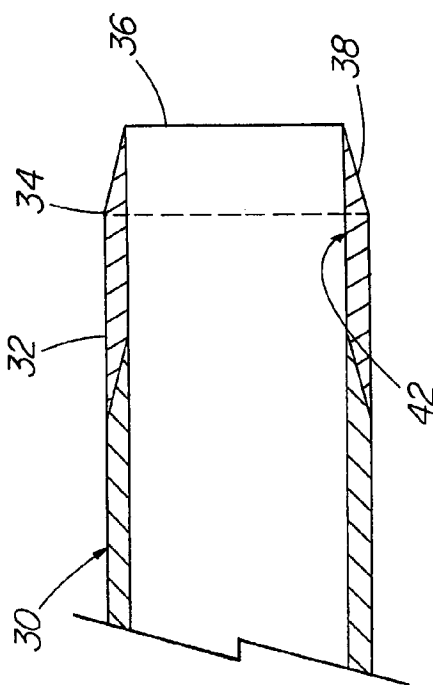
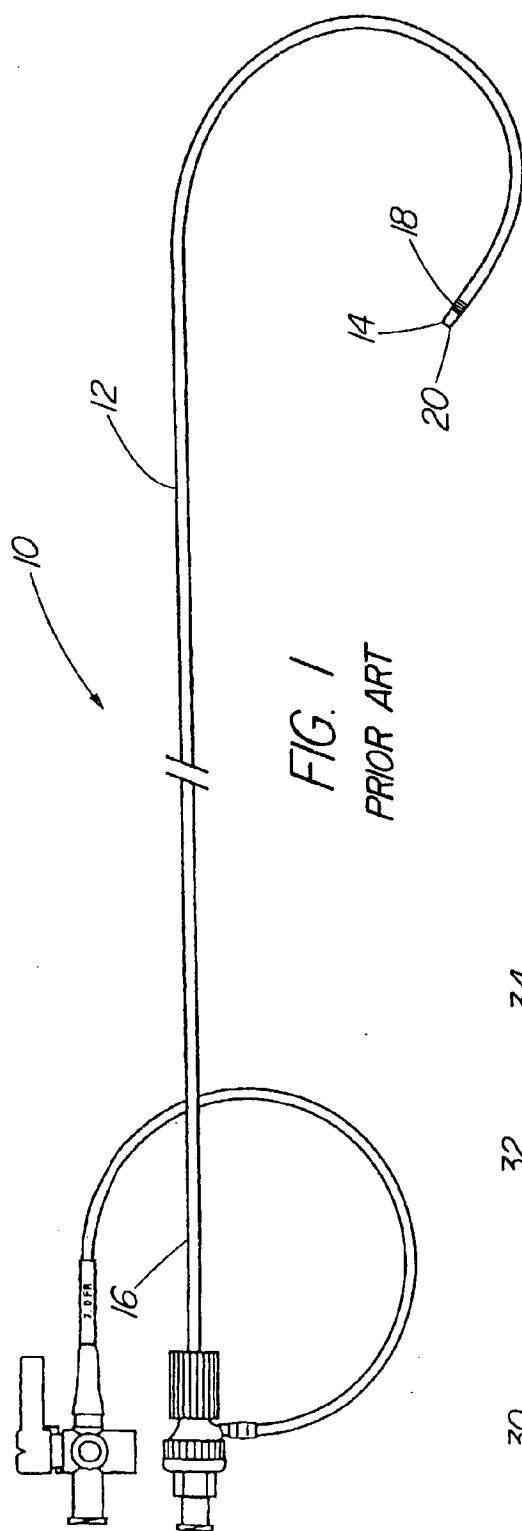
Claims

1. An introducer sheath (30) comprising:
a shaft extending from a proximal end portion to a distal end portion (32);
and
5 a distal tip section (34,40) at said distal end portion (32) of said shaft,
said distal tip section (34,40) comprising a polymeric material containing
over 20% and up to about 75% by weight of radiopaque material, and
said shaft being distinctly less radiopaque than said distal tip section.
2. The introducer sheath (30) according to claim 1, wherein said polymeric
10 material of said distal tip section (34,40) is selected from fluorinated ethylene
propylene, nylon, polyethylene, polyurethane and polytetrafluoroethylene.
3. The introducer sheath (30) according to claim 1 or 2, wherein said distal
tip section (34,40) contains between about 50% to 55% by weight of radiopaque
material, and/or wherein said radiopaque material is selected from the group tungsten,
15 titanium, tantalum, platinum, gold, silver, bismuth trioxide and lead, and/or wherein
said radiopaque material is tungsten particles (46) that range in size from about 1.4
microns to about 1.8 microns.
4. The introducer sheath (30) according to claim 1, wherein said radiopaque
material is tungsten particles (46) that range in size from about 0.5 microns to about
20 25 microns.
5. The introducer sheath (30) according to claim 1, wherein said distal tip
section (40) was initially formed as a separate member, and then was bonded to the
distal end or distal end portion of the shaft, at an intersection thereof.
6. The introducer sheath (30) according to claim 5, wherein the intersection
25 is either stepped or tapered.
7. The introducer sheath (30) according to any of claims 1 to 6, wherein said
polymeric material of said distal tip section (34,40) is fluorinated ethylene propylene
and contains radiopaque filler over 20% by weight of tungsten particles (46).
8. The introducer sheath (30) according to claim 7, wherein said distal tip
30 section (34,40) contains between about 50% to 55% by weight of tungsten
particles (46) that range in size from about 1.4 microns to about 1.8 microns.

- 6 -

9. An introducer sheath (30) comprising:
a shaft extending from a proximal end portion to a distal end portion; and
a distal tip section (34,40) at said distal end portion of said shaft,
said distal tip section comprising a polymeric material containing
5 radiopaque particles,
said shaft being distinctly less radiopaque than said distal tip section,
said distal tip section polymeric material is fluorinated ethylene propylene
and contains between about 20% to 75% by weight of tungsten particles (46) that
range in size from about 1.4 microns to about 1.8 microns.

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INTERNATIONAL SEARCH REPORT

International Application No

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A. CLASSIFICATION OF SUBJECT MATTER
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According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61M A61L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 045 072 A (CASTILLO MIGUEL A ET AL) 3 September 1991 (1991-09-03) cited in the application	1-3,5
A	column 1, line 62 -column 2, line 41; figures	9
X	US 5 300 048 A (DREWES JR DAVID A ET AL) 5 April 1994 (1994-04-05) cited in the application	1-3
A	column 2, line 5 - line 64; figures	9
A	US 5 948 489 A (HOPKINS RONALD J) 7 September 1999 (1999-09-07) claims 1,2; figures	1,3,4,9
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☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

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O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

* & * document member of the same patent family

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INTERNATIONAL SEARCH REPORT

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 4 657 024 A (CONEYS THOMAS A) 14 April 1987 (1987-04-14) column 3, line 16 -column 4, line 4; figures ---	1-3,9
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INTERNATIONAL SEARCH REPORT

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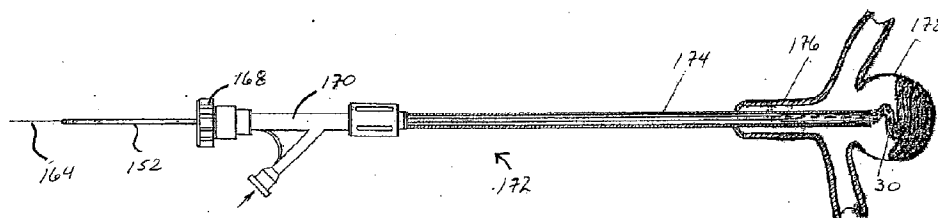
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(54) Title: VASCULAR OCCLUSION DEVICES AND METHODS



(57) Abstract: A device for *in situ* treatment of vascular or cerebral occlusions comprises an occlusion device having a flexible, longitudinally extending elastomeric matrix member that assumes a non-linear shape to conformally fill a targeted site. The occlusion device has one or more longitudinally extending filaments that can be varied to impart properties to the occlusion device.

WO 2006/058042 A2

VASCULAR OCCLUSION DEVICES AND METHODS

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application is based upon and claims the benefit of co-pending, commonly assigned Serial No. 10/998,357, filed November 26, 2004, co-pending, commonly assigned U.S. patent application Serial No. 11/111,487, filed April 21, 2005, and co-pending, commonly assigned U.S. patent application Serial No. 11/229,044, filed September 15, 2005, each of which is incorporated herein by reference in its entirety.

FIELD OF THE INVENTION

[0002] This invention relates to methods and devices for the treatment of vascular aneurysms and other comparable vascular abnormalities. More particularly, this invention relates to occlusion devices for vascular aneurysms that comprise a reticulated elastomeric matrix structure and a delivery device.

BACKGROUND OF THE INVENTION

[0003] The cardiovascular system, when functioning properly, supplies nutrients to all parts of the body and carries waste products away from these parts for elimination. It is essentially a closed system comprising the heart, a pump that supplies pressure to move blood through the blood vessels, blood vessels that lead away from the heart, called arteries, and blood vessels that return blood toward the heart, called veins. On the discharge side of the heart is a large blood vessel called the aorta from which branch many arteries leading to all parts of the body, including the organs. As the arteries get close to the areas they serve, they diminish to small arteries, still smaller arteries called arterioles, and ultimately connect to capillaries. Capillaries are minute vessels where outward diffusion of nutrients, including oxygen, and inward diffusion of wastes, including carbon dioxide, takes place.

[0004] Capillaries connect to tiny veins called venules. Venules in turn connect to larger veins which return the blood to the heart by way of a pair of large blood vessels called the inferior and superior venae cava.

[0005] When the wall 2 of an artery 4 has a weakness, the blood pressure can dilate or expand the region of the artery 4 with the weakness, and a pulsating sac 6 called a berry or saccular aneurysm (Figure 1), can develop. Saccular aneurysms are common at artery bifurcations 8 (Figures 2 and 3) located around the brain. Dissecting aneurysms are common in the thoracic and abdominal aortas. The pressure of an aneurysm against surrounding tissues, especially the pulsations, may cause pain and may also cause tissue damage. However, aneurysms are often asymptomatic. The blood in the vicinity of the aneurysm can become turbulent, leading to formation of blood clots, that may be carried to various body organs where they may cause damage in varying degrees, including cerebrovascular incidents, myocardial infarctions and pulmonary embolisms. Should an aneurysm tear and begin to leak blood, the condition can become life threatening, sometimes being quickly fatal, in a matter of minutes.

[0006] Because there is relatively little blood pressure in a vein, venous “aneurysms” are non-existent. Therefore, the description of the present invention is related to arteries, but applications within a vein, if useful, are to be understood to be within the scope of this invention.

[0007] The causes of aneurysms are still under investigation. However, researchers have identified a gene associated with a weakness in the connective tissue of blood vessels that can lead to an aneurysm. Additional risk factors associated with aneurysms such as hyperlipidemia, atherosclerosis, fatty diet, elevated blood pressure, smoking, trauma, certain infections, certain genetic disorders, such as Marfan’s Syndrome, obesity, and lack of exercise have also been identified. Cerebral aneurysms frequently occur in otherwise healthy and relatively youthful people and have been associated with many untimely deaths.

[0008] Aneurysms, widening of arteries caused by blood pressure acting on a weakened arterial wall, have occurred ever since humans walked the planet. In recent times, many methods have been proposed to treat aneurysms. For example, Greene, Jr., et al., U.S. Patent No. 6,165,193 proposes a vascular implant formed of a compressible foam hydrogel that has a compressed configuration from which it is expansible into a configuration substantially conforming to the shape and size of a vascular malformation to be embolized. The hydrogel of the '193 patent lacks the mechanical properties to enable the hydrogel to regain its size and shape *in vivo* were it to be compressed for catheter, endoscope, or syringe delivery, and the process can be complex and difficult to implement. Other patents disclose introduction of a device, such as a stent or balloon (Naglireiter et al., U.S. Patent No. 6,379,329) into the aneurysm, followed by introduction of a hydrogel in the area of the stent to attempt to repair the defect (Sawhney et al., U.S. Patent No. 6,379,373).

[0009] Ferrera et al., U.S. Published Patent Application No. 2003/0199887 discloses that a porous or textural embolization device comprising a resilient material can be delivered to a situs of a vascular dysfunction. The device has a relaxed state and a stretched state, where the relaxed state forms a predetermined space-filling body.

[0010] Still other patents suggest the introduction into the aneurysm of a device, such as a stent, having a coating of a drug or other bioactive material (Gregory, U.S. Patent No. 6,372,228). Other methods include attempting to repair an aneurysm by introducing via a catheter a self-hardening or self-curing material into the aneurysm. Once the material cures or polymerizes *in situ* into a foam plug, the vessel can be recanalized by placing a lumen through the plug (Hastings, U.S. Patent No. 5,725,568).

[0011] Another group of patents relates more specifically to saccular aneurysms and teaches the introduction of a device, such as string, wire or coiled material (Boock, U.S. Patent No. 6,312,421), or a braided bag of fibers (Greenhalgh, U.S.

Patent No. 6,346,117) into the lumen of the aneurysm to fill the void within the aneurysm. The device introduced can carry hydrogel, drugs, or other bioactive materials to stabilize or reinforce the aneurysm (Greene Jr., et al., U.S. Patent No. 6,299,619).

[0012] Another treatment known to the art comprises catheter delivery of platinum microcoils into the aneurysm cavity in conjunction with an embolizing composition comprising a biocompatible polymer and a biocompatible solvent. The deposited coils or other non-particulate agents are said to act as a lattice about which a polymer precipitate grows thereby embolizing the blood vessel (Evans et al., U.S. Patent No. 6,335,384).

[0013] It is an understanding of the present invention that such methods and devices suffer from a variety of problems. For example, if an aneurysm treatment is to be successful, any implanted device must be present in the body for a long period of time, and must therefore be resistant to rejection and not degrade into materials that cause adverse side effects.¹ While platinum coils may have some benefits in this respect, they are inherently expensive, and the pulsation of blood around the aneurysm may cause difficulties such as migration of the coils, incomplete sealing of the aneurysm, or fragmentation of blood clots. It is also well known that the use of a coil is frequently associated with recanalization of the site, leading to full or partial reversal of the occlusion. If the implant does not fully occlude the aneurysm and effectively seal against the aneurysm wall, pulsating blood may seep around the implant and the distended blood vessel wall causing the aneurysm to reform around the implant.

[0014] The delivery mechanics of many of the known aneurysm treatment methods can be difficult, challenging, and time consuming.

[0015] Most contemporary vascular occlusion devices, such as coils, thrombin, glue, hydrogels, etc., have serious limitations or drawbacks, including, but not limited to, early or late recanalization, incorrect placement or positioning, migration, and lack of tissue ingrowth and biological integration. Also, some of the devices are physiologically unacceptable and engender unacceptable foreign body reactions or rejection. In light of the drawbacks of the known devices and methods, there is a need for more effective aneurysm treatment that produces permanent biological occlusion, can be delivered in a compressed state through small diameter catheters to a target vascular or other site with minimal risk of migration, and/or will prevent the aneurysm from leaking or reforming.

OBJECTS OF THE INVENTION

[0016] It is an object of the invention to provide a method and device for the treatment of vascular aneurysms.

[0017] It is also an object of the invention to provide a method and device for occluding cerebral aneurysms.

[0018] It is a further object of the invention to provide a method and device for occluding cerebral aneurysms by bio-integrating and sealing off the aneurysm to prevent migration, recanalization, leaking, or reforming.

[0019] It is a yet further object of the invention to provide a method and device for occluding vascular aneurysms wherein the device comprises a biocompatible member and a delivery device.

[0020] It is a yet further object of the invention to provide a method and device for occluding vascular aneurysms comprising a biocompatible member and two or more longitudinally extending components.

[0021] It is a yet further object of the invention to provide a system for treating cerebral aneurysms that comprises a reticulated elastomeric matrix structure and a delivery device.

[0022] It is a yet further object of the invention to provide an occlusion device comprising a flexible, longitudinally extending elastomeric matrix member, wherein the device assumes a non-linear shape to conformably fill a targeted vascular site.

[0023] It is a yet further object of the invention to provide an occlusion device comprising an elastomeric matrix and one or more structural filaments.

[0024] It is a yet further object of the invention to provide an occlusion device wherein the structural components comprise platinum wire and polymeric fiber or filament.

[0025] It is a yet further object of the invention to provide a method of preparing an occlusion device comprising an elastomeric matrix and one or more structural filaments.

[0026] It is a yet further object of the invention to provide a method of occluding a vascular aneurysm wherein an occlusion device comprising an elastomeric matrix and one or more structural filaments conformally fills a targeted vascular site.

[0027] These and other objects of the invention will become more apparent in the discussion below.

SUMMARY OF THE INVENTION

[0028] According to the invention an aneurysm treatment device is provided for *in situ* treatment of aneurysms, particularly, cerebral aneurysms, in mammals, especially humans. The treatment device comprises a resiliently implant comprised of a reticulated, biodurable elastomeric matrix and one or more structural filaments, wherein the implant is deliverable into the aneurysm, for example, by being loadable into a catheter and passed through a patient's vasculature. Pursuant to the invention, useful aneurysm treatment devices can have sufficient resilience, or other mechanical properties, including expansion, to conformally fill the space within the aneurysm sac and to occlude the aneurysm.

[0029] In another embodiment of the invention, an implant comprises one or more flexible, connected, preferably spherically-, ellipsoidally-, or cylindrically-shaped structures that are positioned in a stretched state in a delivery catheter. The connected structures preferably have spring coils on each end, one of which coils is releasably secured within the delivery catheter.

[0030] In another embodiment of the invention, an implant for occlusion of an aneurysm comprises reticulated elastomeric matrix in a shape that can be inserted into a delivery catheter, can be ejected or deployed from the delivery catheter into an aneurysm, and can then be of sufficient size and shape to conformally fill and occlude the aneurysm. Examples of such shapes include, but are not limited to, cylinders, hollow cylinders, noodles, hollow cylinders with lateral slots, rods, tubes, or elongated prismatic forms, coiled, helical or other more compact configurations, segmented cylinders where "sausage-like" segments have been formed, braided shapes, or flat spiral shapes, optionally with one or more structural filaments such as polymeric fiber or filament or radiopaque wire support extending therein.

[0031] In another embodiment of the invention, an aneurysm occlusion device comprises elastomeric matrix in the nature of a string or other elongate form and having one or more structural filaments. Preferably the filaments comprise one or more platinum wires and polymeric fiber or filament. The occlusion device may optionally have lateral components to impart chain-like behavior when the occlusion device is advanced to conformally fill an aneurysm sac or cavity.

[0032] Although multiple implants can be deployed, used, or implanted, it is a feature of one aspect of the present invention that preferably a single implant fills an aneurysm, effectively a "single shot" occlusion. It is contemplated, in one embodiment, that even when their pores become partially filled or completely filled with biological fluids, bodily fluids and/or tissue in the course of time or immediately after delivery, and/or the implants are either still partially compressed or partially recovered after delivery, such implantable device or devices for vascular malformation applications have a volume, prior to packing *in vivo*, of at least about 50% of the aneurysm volume. The ratio of implant (or implants) volume to aneurysm volume is defined as packing density. In another embodiment, such implantable device or devices for vascular malformation applications have a volume, prior to packing *in vivo*, of at least about 75% of the aneurysm volume. In another embodiment, such implantable device or devices for vascular malformation applications have a volume, prior to packing *in vivo*, of at least about 125 % of the aneurysm volume. In another embodiment, such implantable device or devices for vascular malformation applications have a volume, prior to packing *in vivo*, of at least about 175% of the aneurysm volume. In another embodiment, such implantable device or devices for vascular malformation applications have a volume, prior to packing *in vivo*, of at least about 200 % of the aneurysm volume.

[0033] The packing density is targeted to achieve angiographic occlusion after embolization of the aneurysm by the implant, followed by clotting, thrombosis, and tissue ingrowth, ultimately leading to biological obliteration of the aneurysm sac. Permanent tissue ingrowth will prevent any possible recanalization or migration.

[0034] It is furthermore preferable that the implant be treated or formed of a material that will encourage such fibroblast immigration. It is also desirable that the implant be configured, with regard to its three-dimensional shape, and its size, resiliency and other physical characteristics, and be suitably chemically or biochemically constituted to foster eventual tissue ingrowth and formation of scar tissue that will help conformally fill the aneurysm sac.

[0035] The aneurysm treatment according to the invention device comprises, in one embodiment, a reticulated biodurable elastomeric matrix or the like that is capable of being inserted into a catheter for implantation. In another embodiment, the implant can be formed of a partially hydrophobic reticulated biodurable elastomeric matrix having its pore surfaces coated to be partially hydrophilic, for example, by being coated with at least a partially hydrophilic material, optionally a partially hydrophilic reticulated elastomeric matrix. The entire elastomeric matrix may have such a hydrophilic coating throughout the pores of the reticulated elastomeric matrix.

[0036] In one embodiment, the hydrophilic material carries a pharmacologic agent, for example, elastin or fibrin to foster fibroblast proliferation. It is also within the scope of the invention for the pharmacologic agent to include sclerotic agents, inflammatory induction agents, growth factors capable of fostering fibroblast proliferation, or genetically engineered an/or genetically acting therapeutics. The pharmacologic agent or agents preferably are dispensed over time by the implant. Incorporation of biologically active agents in the hydrophilic phase of a composite foam suitable for use in the practice of the present invention is described in co-pending, commonly assigned U.S. patent applications Serial No. 10/692,055, filed October 22, 2003, Serial No. 10/749,742, filed December 30, 2003 (published

February 24, 2005 as U.S. Patent Publication No. 20050043585), Serial No. 10/848,624, filed May 17, 2004 (published February 24, 2005 as U.S. Patent Publication No. 20050043816), and Serial No. 10/900,982, filed July 27, 2004, each of which is incorporated herein by reference in its entirety.

[0037] In another aspect, the invention provides a method of treating an aneurysm comprising the steps of:

- imaging an aneurysm to be treated to determine its size and topography;
- selecting an aneurysm treatment device according to the invention for use in treating the aneurysm; and
- implanting the aneurysm treatment device into the aneurysm.

[0038] Preferably, the method further comprises:

- loading the aneurysm treatment device into a catheter or other delivery means;
- threading the catheter through an artery to the aneurysm; and
- positioning and releasing the aneurysm treatment device in the aneurysm.

[0039] Once an aneurysm has been identified using suitable imaging technology, such as a magnetic resonance image (MRI), computerized tomography scan (CT Scan), x-ray imaging with contrast material or ultrasound, and is to be treated, the surgeon chooses which implant he or she feels would best suit the aneurysm, both in shape and size. The implant can be used alone. In another embodiment, the aneurysm treatment device of the invention may also be used in conjunction with a frame of platinum coils or with a stent or balloon across the neck of the aneurysm, to assist in reducing or eliminating the risk of implant migration out of the neck of the aneurysm. This is particularly true in the case of wide neck or giant aneurysms. The chosen implant is then loaded into an intravascular catheter in a linear state. If desired, the implant can be provided in a sterile package in a pre-loaded configuration, ready for loading into a catheter. Alternatively, the implants can

be made available in an expanded state, also, preferably, in a sterile package, and the surgeon at the site of implantation can use a suitable secondary device or a loader apparatus to compress an implant so that it can be loaded into a delivery catheter.

[0040] With an implant loaded into the catheter, the catheter is advanced through an artery to the diseased portion of the affected artery using any suitable technique known in the art. By use of the catheter the implant is then inserted and positioned within the aneurysm. As the implant is released from the catheter, where it is manipulated into a suitable position within the aneurysm.

[0041] In another embodiment of the invention, an occlusion device comprises a flexible, longitudinally extending elastomeric matrix member, wherein the device assumes a non-linear shape capable of conformally filling a targeted vascular site.

[0042] In another embodiment of a device of the invention, an occlusion device also comprises at least one longitudinally extending reinforcing filament or fiber.

[0043] In another embodiment of a device of the invention, each filament or fiber is selected from the group consisting of platinum wire, platinum coil, platinum hypo-tube, platinum band, polymeric fiber or filament, a braid of platinum wire and polymeric fiber or filament, and a braid of two or more platinum wires.

[0044] In another embodiment of a device of the invention, each reinforcing filament or fiber is inserted into the elastomeric matrix member.

[0045] In another embodiment of a device of the invention, the elastomeric matrix member is adhered to each reinforcing filament or fiber.

[0046] In another embodiment of a device of the invention, there are at least two reinforcing filaments or fibers.

[0047] In another embodiment of a device of the invention, the reinforcing filaments or fibers are knotted or looped together at various points to secure the elastomeric matrix member.

[0048] In another embodiment of a device of the invention, the reinforcing filaments or fibers are knotted together by radiopaque bands.

[0049] In another embodiment of a device of the invention, at least one reinforcing filament or fiber is radiopaque.

[0050] In another embodiment of a device of the invention, the elastomeric matrix is a biodegradable, reticulated elastomeric matrix.

[0051] In another embodiment of a device of the invention, the elastomeric matrix is a polycarbonate polyurethane-urea, polycarbonate polyurea-urethane, polycarbonate polyurethane, or polycarbonate polysiloxane polyurethane.

[0052] In another embodiment of a device of the invention, the elastomeric matrix is resiliently recoverable.

[0053] In another embodiment of the invention, a method of occluding an aneurysm or vessel comprises deploying or inserting a device of the invention into an aneurysm or vessel.

[0054] In another embodiment of the invention, a packaging or introducer system comprises:

an introducer sheath having a longitudinally extending lumen and proximal and distal ends;

an occlusion device of the invention positioned within said lumen, said occlusion device having a proximal end;

a side arm attached to the proximal end of the introducer sheath and having a hemostasis valve and a flusher port; and

a pusher member extending through the hemostasis valve into the introducer sheath and having a distal end removably engaged to the proximal end of the occlusion device.

[0055] In another embodiment of a packaging or introducer system of the invention, an interlocking wire having a distal end extends longitudinally into the pusher member, the occlusion device has a loop at its proximal end, the distal end of the pusher member has an opening through which said loop extends, the distal end of the interlocking wire is releasably held within the distal end of the pusher member, and the distal end of the interlocking wire releasably engages said loop so that the distal end of the pusher member releasably engages the proximal end of the occlusion device.

[0056] In another embodiment of a packaging or introducer system of the invention, the distal end of the interlocking wire and the distal end of the pusher member are both radiopaque.

[0057] In another embodiment of the invention, a method for occluding a vessel or aneurysm comprises:

introducing an introducer system of the invention into a delivery catheter having a longitudinally extending lumen and proximal and distal ends with hydraulic assistance;

withdrawing the introducer sheath and side arm, leaving the occlusion device positioned within the lumen of the delivery catheter;

advancing the occlusion device using the pusher member and hydraulic assistance to position the occlusion device within a targeted vascular site;

disengaging the pusher member from the occlusion device; and
withdrawing the pusher member.

[0058] In another embodiment of the invention, a vascular occlusion device comprises:

a flexible, longitudinally extending biocompatible member, and at least one longitudinally extending component engaged with the biocompatible member, optionally at one or more points, to secure the biocompatible member and assist it in conformally filling a targeted vascular site.

[0059] In another embodiment of the invention, the device assumes a non-linear shape to conformally fill a targeted vascular site.

[0060] In another embodiment of the invention, the device comprises a non-curvilinear shape in at least one portion of the member.

[0061] In another embodiment of a device of the invention, the non-curvilinear shape comprises at least one vertex.

[0062] In another embodiment of a device of the invention, the at least one vertex comprises a plurality of vertices.

[0063] In another embodiment of a device of the invention, the plurality of vertices permit chain-like folding of the device.

[0064] In another embodiment of a device of the invention, the biocompatible member comprises an elastomeric matrix.

[0065] In another embodiment of a device of the invention, the elastomeric matrix is a biodurable, reticulated elastomeric matrix.

[0066] In another embodiment of a device of the invention, the elastomeric matrix is selected from the group consisting of polycarbonate polyurethane-urea, polycarbonate polyurea-urethane, polycarbonate polyurethane, and polycarbonate polysiloxane polyurethane.

[0067] In another embodiment of a device of the invention, the elastomeric matrix comprises resiliently recoverable material.

[0068] In another embodiment of a device of the invention, each longitudinally extending component comprises a structural filament.

[0069] In another embodiment of a device of the invention, the at least one longitudinally extending components comprise a polymeric fiber or filament and at least one wire element.

[0070] In another embodiment of a device of the invention, the at least one wire element comprises a continuous wire.

[0071] In another embodiment of a device of the invention, the at least one wire element comprises a plurality of staples, preferably interlocked to form a chain.

[0072] In another embodiment of the invention, the device comprises at least two longitudinally extending components that are coupled to each other at a plurality of locations.

[0073] In another embodiment of a device of the invention, the components are coupled by knotting.

[0074] In another embodiment of a device of the invention, the at least one longitudinally extending components comprise at least two structural filaments or fibers.

[0075] In another embodiment of a device of the invention, there are two structural filaments or fibers.

[0076] In another embodiment of a device of the invention, the structural filaments or fibers are selected from materials preselected to vary at least one physical property of the device.

[0077] In another embodiment of a device of the invention, the physical property is stiffness.

[0078] In another embodiment of a device of the invention, the physical property comprises modulus of elasticity.

[0079] In another embodiment of a device of the invention, each structural filament or fiber is selected from the group consisting of platinum wire, polymeric fiber or filament, a braid of platinum wire and polymeric fiber or filament, and a braid of two or more platinum wires.

[0080] In another embodiment of a device of the invention, the structural filaments are knotted together by radiopaque bands.

[0081] In another embodiment of a device of the invention, at least one longitudinally extending component is radiopaque.

[0082] In another embodiment of a device of the invention, the material of each component and the coupling between the at least two components are selected to produce a desired physical property of the device.

[0083] In another embodiment of the invention, the desired physical property of the device comprises stiffness at a location of coupling or engaging and the stiffness comprises a stiffness relative to a stiffness of the device at a point substantially distant from the point of coupling or engaging.

[0084] In another embodiment of the invention, the stiffness as measured at the point of coupling or engaging is measured relative to a stiffness of the device at a point substantially distant from the point of coupling or engaging.

[0085] In another embodiment of the invention, the device is capable of occluding an aneurysm, such as a cerebral aneurysm.

[0086] In another embodiment of the invention, the device is capable of occluding a vessel or vascular malformation.

[0087] In another embodiment of the invention, an introducer system for a vascular occlusion device, the vascular occlusion device having a proximal end and a distal end, the distal end having a contact element coupled to it, comprises:

an introducer component having a longitudinally extending lumen and proximal and distal ends;

a pusher component slidable within the introducer component, the pusher component having a distal end positioned adjacent to the distal end of the occlusion device; and

a core component having a distal end and extending through the pusher component and parallel to the occlusion device so that the distal end of the core component contacts the contact element, thereby applying a tensile force to the occlusion device.

[0088] In another embodiment of the invention, an introducer system further comprises:

an interlocking wire having a distal end extending longitudinally into the pusher member,

wherein:

the occlusion device has a release element at its proximal end,

the distal end of the pusher component has an opening through which the release element extends,

the distal end of the interlocking wire is releasably held within the distal end of the pusher member, and

the distal end of the interlocking wire releasably engages the release element so that the distal end of the pusher component releasably engages the proximal end of the occlusion device.

[0089] In another embodiment of an introducer system of the invention, the release element comprises a loop.

[0090] In another embodiment of an introducer system of the invention, the contact element is a tensioning element.

[0091] In another embodiment of the invention, a method for occluding a targeted vascular site comprises:

introducing an introducer system into a delivery catheter having a longitudinally extending lumen and proximal and distal ends, the introducer system carrying a vascular occlusion device and having a pusher component;

withdrawing the introducer system, leaving the vascular occlusion device positioned within the lumen of the delivery catheter;

advancing the vascular occlusion device using the pusher component to position the vascular occlusion device within the targeted vascular site;

disengaging the pusher component from the occlusion device; and
withdrawing the pusher.

[0092] In another embodiment of the invention, a device for occluding a targeted vascular site comprises:

an elongate occluding element comprising a material permitting ingrowth of tissue at the targeted vascular site; and

a plurality of features provided along the occluding element, optionally at preselected locations, the features selected to confer material characteristics allowing the creation of vertices in the element.

[0093] In another embodiment of a device of the invention, the vertices are at least temporary.

[0094] In another embodiment of a device of the invention, the vertices facilitate packing of the occluding element into the targeted vascular site.

[0095] In another embodiment of a device of the invention, at least one of the features comprises a topological characteristic of the elongate element.

[0096] In another embodiment of the invention, the device further comprises a second element coupled to the elongate element, wherein at least one of the features comprises topological characteristic of the second element.

[0097] In another embodiment of a device of the invention, the device further comprises a third element coupled to the elongate element, wherein at least one of the features comprises a relationship between the second and third elements.

[0098] In another embodiment of a device of the invention, the elongate element comprises a biodurable material permitting vascular tissue ingrowth and the second element comprises a polymeric fiber or filament.

[0099] In another embodiment of a device of the invention, the topological characteristic of the polymeric fiber or filament comprises a stitch.

[00100] In another embodiment of a device of the invention, the relationship between the second and third elements comprises a knot.

[00101] In another embodiment of a device of the invention, at least one of the group consisting of a dimension of a feature and a distance between a pair of features is preselected to facilitate packing of the targeted vascular site.

[00102] In another embodiment of the invention, a method for treating a condition at a targeted vascular site comprises the steps of:

providing an elongate occlusion device comprising biocompatible material;

introducing the occlusion device into the targeted vascular site; and

while introducing the occlusion device, inducing at least one non-curvilinear geometry in the occlusion device.

[00103] In another embodiment of a method of the invention, the step of inducing at least one non-curvilinear geometry produces a geometry of the occlusion

device that packs the targeted vascular site in a substantially conformal manner.

[00104] In another embodiment of a method of the invention, the at least one non-curvilinear geometry comprises a plurality of folds.

[00105] In another embodiment of a method of the invention, the step of inducing a plurality of folds produces a chain-like occlusion device for packing the targeted vascular site in a substantially conformal manner.

[00106] In another embodiment of a method of the invention, the occlusion device comprises a biocompatible material.

[00107] In another embodiment of a method of the invention, the biocompatible material comprises a material permitting ingrowth of tissue at the targeted site.

[00108] In another embodiment of a method of the invention, the occlusion device is introduced to permanently biointegrate at the targeted site.

[00109] In another embodiment of the invention, a method for treating an aneurysm in a mammal comprises the steps of:

providing an elongate biocompatible, biodurable material permitting tissue ingrowth at the site of the aneurysm; and

introducing the biocompatible, biodurable material at the site of the aneurysm in a quantity sufficient to occlude the aneurysm and to permit permanent biointegration of the occlusion device in the aneurysm.

[00110] In another embodiment of the invention, the biocompatible, biodurable material is a reticulated elastomeric matrix.

[00111] In another embodiment of the invention, a method for treating a cerebral aneurysm comprises the step of introducing sufficient biocompatible material into the cerebral aneurysm to pack the aneurysm with the material to a packing density of from at least about 10% to at least about 200%.

[00112] In another embodiment of a method of the invention, the biocompatible material comprises a flexible, longitudinally extending biocompatible member.

[00113] In another embodiment of a method of the invention, the biocompatible material comprises non-swellable material.

[00114] In another embodiment of the invention, a mechanism for detaching a vascular implant from a delivery device, the vascular implant having a proximal end and a coupling component at its proximal end, comprises:

an engagement element coupled at a distal end of the delivery device, the engagement element having a first, engaged position and a second, disengaged position; and

an energy transfer component coupled to the engagement element at a distal portion of the component to actuate the engagement element,

wherein the engagement element, when actuated, engages the coupling component of the implant when in the first position and releases the coupling component when in the second position.

[00115] In another embodiment of a mechanism of the invention, the coupling component of the implant comprises a flexible structure.

[00116] In another embodiment of a mechanism of the invention, the flexible structure comprises at least one opening through which an aspect of the engagement element of the delivery device may pass when in the first, engaged position.

[00117] In another embodiment of a mechanism of the invention, the flexible structure comprises a loop.

[00118] In another embodiment of a mechanism of the invention, the engagement element comprises a structure that moves, along an axis, from the first position to the second position.

[00119] In another embodiment of a mechanism of the invention, the delivery device comprises at least one of the group consisting of a wire and a sheath, the axis is parallel to the longitudinal axis of the delivery device, and the energy transfer component comprises at least one of the wire and the sheath.

[00120] In another embodiment of a mechanism of the invention, the delivery device comprises a sheath and the energy transfer component comprises a wire, and the engagement element transitions between the first position and the second position as a result of a relative rotation of the wire engagement element with respect to the delivery device sheath.

[00121] In another embodiment of a mechanism of the invention, the engagement element comprises a distal portion of the wire, the coupling component of the implant comprises a loop structure, and, in the first position of the engagement element, the loop structure is stably retained about a distal portion of the wire and, in the second position of the engagement element, the loop structure is released over a free distal end of the wire.

[00122] In another embodiment of a mechanism of the invention,
the distal portion of the wire has threads that engage mating threads coupled to the sheath,
the delivery device comprises a distal portion having a side wall with an aperture through which the loop structure passes and is held in place when the engagement element is in the first position, and
when the engagement element is in the second position, the distal end of the wire is proximal of the aperture, releasing the loop structure and allowing it to exit through the aperture.

[00123] In another embodiment of a mechanism of the invention, the control element is operable by a practitioner.

[00124] In another embodiment of the invention, a method for fabricating a vascular occlusion device comprises the steps of:

providing a biocompatible material adapted for tissue ingrowth and capable of being formed into at least one elongate element having a longitudinal axis and dimensioned for vascular insertion;

engaging at least one support element with the biocompatible material to at least partially lie substantially along at least a portion of the longitudinal axis of the at least one elongate element; and

forming the elongate element from the biocompatible material substantially in the vicinity of the longitudinal axis.

[00125] In another embodiment of a method of the invention, the elongate element comprises a flexible linear element.

[00126] In another embodiment of a method of the invention, the at least one support element comprises a structural filament engaged with the biocompatible material substantially along at least a portion of its longitudinal axis.

[00127] In another embodiment of a method of the invention, the at least one support element comprises polymeric fiber or filament.

[00128] In another embodiment of a method of the invention, the polymeric fiber or filament is stitched to the biocompatible material.

[00129] In another embodiment of a method of the invention, the polymeric fiber or filament is engaged with the biocompatible material with at least one adhesive.

[00130] In another embodiment of a method of the invention, the stitching is performed by a sewing machine.

[00131] In another embodiment of a method of the invention, the at least one support element further comprises a second support element.

[00132] In another embodiment of a method of the invention, the second support element comprises a staple.

[00133] In another embodiment of a method of the invention, the at least one support element comprises at least two staples interlocking with one another to form a chain.

[00134] In another embodiment of a method of the invention, the at least one second support element comprises a radiopaque material.

[00135] In another embodiment of a method of the invention, the at least one second support element comprises wire.

[00136] In another embodiment of a method of the invention, the wire is coupled to the polymeric fiber or filament at a plurality of points.

[00137] In another embodiment of a method of the invention, the coupling at at least one of the plurality of points comprises a knot.

[00138] In another embodiment of a method of the invention, the at least one support element comprises at least two elements including a braided platinum wire/polymeric fiber or filament filament subassembly and a polymeric fiber or filament element.

[00139] In another embodiment of a method of the invention, the at least second support element comprises a plurality of staples.

[00140] In another embodiment of a method of the invention the staples are spaced apart from one another.

[00141] In another embodiment of a method of the invention, the step of forming the elongate element from the biocompatible material and the engaged support element comprises separating the elongate element and the support element from adjoining material.

[00142] In another embodiment of a method of the invention, the step of separating is accomplished by cutting.

[00143] In another embodiment of a method of the invention, the method further comprises the step of removing excess material so that the elongate element has a preselected maximum width.

[00144] In another embodiment of a method of the invention, the method further comprises the step of coupling a visualizable element proximate to the end of the elongate element.

[00145] In another embodiment of a method of the invention, the visualizable end unit comprises a coil.

[00146] In another embodiment of a method of the invention, the end unit comprises a radiopaque material.

[00147] In another embodiment of a method of the invention, the length of the elongate element is from about 1 mm to about 1500 mm, preferably from about 50 mm to about 250 mm.

[00148] In another embodiment of a method of the invention, the width of the elongate member is from about 0.25 mm to about 12 mm, preferably from about 0.25 mm to about 0.5 mm.

[00149] In another embodiment of a method of the invention, the biocompatible material comprises an elastomeric matrix sheet material having a thickness of from about 1 mm to about 2 mm.

[00150] In another embodiment of a method of the invention, the stitching of the suture to the biocompatible material forms a continuous stitch line from about 100 mm to about 500 mm long.

[00151] In another embodiment of a method of the invention, the step of engaging at least one support element with the biocompatible material precedes the step of forming the elongate element from the biocompatible material, whereby the elongate element so formed includes the at least one support element.

[00152] In another embodiment of a method of the invention, the step of forming the elongate element from the biocompatible material precedes the step of engaging at least one support element with the biocompatible material.

[00153] In another embodiment of the invention, a method for treating an aneurysm comprises the steps of:

providing a biocompatible element having a form having at least one portion that lacks a predefined geometry; and
introducing the biocompatible element to conformally fill the aneurysm.

[00154] In another embodiment of a method of the invention, the step of introducing the biocompatible material comprises application of the material to a wall of the aneurysm in such a manner that material curves upon itself to produce segments of the material.

[00155] In another embodiment of a method of the invention, the material segments so applied are arranged in a brush stroke form.

[00156] In another embodiment of a method of the invention, the segments, although substantially parallel to the wall of the aneurysm, each have a spatial orientation, and the spatial orientations of the segments are substantially randomly distributed with respect to one another.

[00157] In another embodiment of a method of the invention, the segments are defined *in situ* by vertices in the material.

[00158] In another embodiment of a method of the invention, the segments are defined by curved portions of the material that lack vertices.

[00159] In another embodiment of a method of the invention, the step of introducing the material to conformally fill the aneurysm comprises application of a first layer of the material directly adjacent a wall of the aneurysm and a second layer substantially overlaying the first layer.

[00160] In another embodiment of the invention, a method further comprises the steps of applying additional layers until the aneurysm is substantially occluded.

[00161] In another embodiment of a method of the invention, the step of introducing the biocompatible element to fill the aneurysm comprises the deposition of the material in the manner of a viscous liquid flow.

[00162] In another embodiment of a method of the invention, the material has a stiffness preselected to produce, when the material is fully introduced into the aneurysm, a packing density in a preselected range.

[00163] In another embodiment of a method of the invention, the packing density of the biocompatible material is from at least about 10% to at least about 200%.

[00164] In another embodiment of a method of the invention, the step of introducing the biocompatible material to fill the aneurysm comprises the deposition of the material in the manner of a piece of cooked spaghetti to form a string ball in the aneurysm.

[00165] In another embodiment of the invention, a vascular occlusion device comprises a string-shaped biocompatible element having a plurality of concavities for accommodating ingrowth of vascular tissue.

[00166] In another embodiment of a device of the invention, the concavities comprise pores.

[00167] In another embodiment of a device of the invention, the concavities together form a honeycomb structure.

[00168] In another embodiment of a device of the invention, the concavities together form a reticulated porous structure.

[00169] In another embodiment of a device of the invention, the concavities comprise a plurality of fragmentary pores.

[00170] In another embodiment of the invention, a vascular occlusion device substantially excludes complete pores.

[00171] In another embodiment of a device of the invention, the concavities comprise cavities.

[00172] In another embodiment of a device of the invention, the concavities comprise concave surfaces formed in the exterior surface of a member.

[00173] In another embodiment of a device of the invention, when the member is packed into an aneurysm, concavities are positioned adjacent one another and at least some of the adjacent concavities in neighboring portions of the member together form virtual pores to accommodate tissue ingrowth.

[00174] In another embodiment of a device of the invention, wherein the average largest transverse dimension of the concavities is at least about 50 μm .

[00175] In another embodiment of a device of the invention, the average largest transverse dimension of concavities is at least about 100 μm .

[00176] In another embodiment of a device of the invention, the average largest transverse dimension of concavities is at least about 150 μm .

[00177] In another embodiment of a device of the invention, the average largest transverse dimension of concavities is at least about 200 μm .

[00178] In another embodiment of a device of the invention, the average largest transverse dimension of concavities is at least about 250 μm .

[00179] In another embodiment of a device of the invention, the average largest transverse dimension of concavities is greater than about 250 μm .

[00180] In another embodiment of a device of the invention, the average largest transverse dimension of concavities is at least about 275 μm .

[00181] In another embodiment of a device of the invention, the average largest transverse dimension of concavities is at least about 300 μm .

[00182] In another embodiment of a device of the invention, the average largest transverse dimension of concavities is greater than about 300 μm .

[00183] In another embodiment of a device of the invention, the average largest transverse dimension of concavities is not greater than about 500 μm .

[00184] In another embodiment of a device of the invention, the average largest transverse dimension of the concavities is from about 200 to about 500 microns.

[00185] In another embodiment of the invention, a vascular occlusion device comprises:

a flexible, longitudinally extending biocompatible member for delivery through a lumen of a delivery device,

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the member comprising a plurality of pores having a dimensional characteristic selected on the basis of a minimum interior dimension of the lumen.

[00186] In another embodiment of a device of the invention, the interior dimension of the lumen comprises the inner diameter of the lumen, and the member has a maximum width less than the minimum interior dimension of the lumen.

[00187] In another embodiment of a device of the invention, the pore size is selected in order that the average pore diameter is greater than or equal to about 25% of the maximum width of the member.

[00188] In another embodiment of a device of the invention, the pore size is selected in order that the average pore diameter is from about 25% to about 33% of the maximum diameter of the member.

[00189] In another embodiment of the invention, a system for adjusting the properties of a longitudinally extending device comprise (a) a flexible, longitudinally extending member and (b) at least one longitudinally extending filament engaged with member (a), optionally at various points, wherein component (b) comprises one or more materials preselected to vary at least one physical property of the device.

[00190] In another embodiment of a device of the invention, member (a) is biocompatible.

[00191] In another embodiment of a device of the invention, component (b) is selected from the group consisting of platinum, iridium, and multi-filament polymers.

[00192] In another embodiment of a device of the invention, there are at least two longitudinally extending components.

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BRIEF DESCRIPTION OF THE DRAWINGS

[00193] One or more embodiments of the invention and of making and using the invention, as well as the best mode contemplated of carrying out the invention, are described in detail below, by way of example, with reference to the accompanying drawings, in which:

[00194] Figure 1 is a longitudinal cross-section of an artery with a saccular aneurysm;

[00195] Figure 2 is a top view of an artery at a bifurcation;

[00196] Figure 3 is a top view of an artery at a bifurcation with a saccular aneurysm at the point of bifurcation;

[00197] Figures 4 to 15 represent embodiments of implant systems useful according to the invention;

[00198] Figures 16 to 18 represent an embodiment of the fill/packing behavior (breaking/bending/folding) of an implant system of the invention upon deployment in an aneurysm.

[00199] Figures 19 to 21 represent an embodiment of a delivery system for stiffer implants according to the invention.

[00200] Figure 22 represents an embodiment of a coaxial delivery system for softer implants;

[00201] Figures 23 and 24 represent an embodiment of a suture loop mechanical detachment system;

[00202] Figures 25 and 26 represent micrographs of tissue ingrowth;

[00203] Figures 27A to 27C represent different stages of embolization formation in a dog; and

[00204] Figures 28A to 28C are micrographs of sections of aneurysms treated with an implant of the invention.

DETAILED DESCRIPTION OF THE INVENTION

[00205] There is a need in medicine, as recognized by the present invention, for atraumatic implantable devices that can be delivered to an *in vivo* patient site, for example, a site in a human patient, that can occupy that site for extended periods of time without being harmful to the host. In one embodiment, such implantable devices can also eventually become biologically integrated, for example, ingrown with tissue. Various implants have long been considered potentially useful for local *in situ* delivery of biologically active agents and more recently have been contemplated as useful for control of endovascular conditions including potentially life-threatening conditions such as cerebral and aortic abdominal aneurysms, arteriovenous malfunction, arterial embolization, or other vascular abnormalities.

[00206] The present invention relates to a system and method for treating aneurysms, particularly cerebral aneurysms, *in situ* and *in vivo*. As will be described in detail below, the present invention provides in at least one embodiment a vascular occlusion device comprising a flexible, longitudinally extending biocompatible member and one or more longitudinally extending components coupled to the biocompatible member. In another embodiment of the invention an aneurysm treatment device comprises a reticulated, biodurable elastomeric matrix implant designed to be permanently inserted into an aneurysm with the assistance of an intravascular catheter. Reticulated matrix, from which the implants are preferably made, has sufficient and required liquid permeability and thus permit blood, or other appropriate bodily fluid, and cells and tissues to access interior surfaces of the implants. This happens due to the presence of inter-connected and inter-communicating, reticulated open pores and/or voids and/or channels and/or concavities that form fluid passageways or fluid permeability providing fluid access all through. The implants described in detail below can be made in a variety of sizes and shapes, the surgeon being able to choose the best size and shape to treat a patient's aneurysm. Once inserted, the inventive aneurysm treatment device or

implant is designed to cause angiographic occlusion, followed by clotting, thrombosis, and eventually bio-integration through tissue ingrowth and proliferation.

Furthermore, the inventive aneurysm treatment device can carry one or more of a wide range of beneficial drugs and chemical moieties that can be released at the affected site for various treatments, such as to aid in healing, foster scarring of the aneurysm, prevent further damage, or reduce risk of treatment failure. With release of these drugs and chemicals locally, employing the devices and methods of the invention, their systemic side effects are reduced.

[00207] An implant or occlusion device according to at least one embodiment of the invention comprises a reticulated biodurable elastomeric matrix or other suitable material and structural filaments and can be designed to be inserted into an aneurysm through a catheter. A preferred reticulated elastomeric matrix is an optionally compressible, lightweight material, designed for its ability to expand preferably in conformal fashion within the aneurysm without expanding too much and tearing the aneurysm. In another embodiment, preferred reticulated elastomeric matrix is an optionally compressible, lightweight material, designed for its ability to pack preferably in conformal fashion within the aneurysm without expanding or without any significant expansion and without tearing the aneurysm. Although multiple implants can be deployed, used, or implanted, preferably five or less implants should fill the aneurysm to achieve angiographic occlusion. In another embodiment, preferably ten or less implants should fill the aneurysm to achieve angiographic occlusion. The ratio of implant (or implants) volume to aneurysm volume is defined as packing density. It is contemplated, in one embodiment, that even when their pores become partially filled or completely filled with biological fluids, bodily fluids and/or tissue in the course of time or immediately after delivery, and/or the implants are either still partially compressed or partially recovered after delivery, such implantable device or devices for vascular malformation applications have a volume of at least about 10% of the aneurysm volume. In another embodiment, such implantable device or devices for vascular malformation applications have a volume, prior to packing in

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vivo, of at least about 25% of the aneurysm volume. In another embodiment, such implantable device or devices for vascular malformation applications have a volume, prior to packing *in vivo*, of at least about 50% of the aneurysm volume. In another embodiment, such implantable device or devices for vascular malformation applications have a volume, prior to packing *in vivo*, of at least about 75% of the aneurysm volume. In another embodiment, such implantable device or devices for vascular malformation applications have a volume, prior to packing *in vivo*, of at least about 100 % of the aneurysm volume. In another embodiment, such implantable device or devices for vascular malformation applications have a volume, prior to packing *in vivo*, of at least about 125 % of the aneurysm volume. In another embodiment, such implantable device or devices for vascular malformation applications have a volume, prior to packing *in vivo*, of at least about 175% of the aneurysm volume. In another embodiment, such implantable device or devices for vascular malformation applications have a volume, prior to packing *in vivo*, of at least about 200 % of the aneurysm volume. Insertion of the implant followed by tissue ingrowth should result in total obliteration of the aneurysm sac.

[00208] It would be desirable to have an implantable system which, e.g., can optionally cause immediate thrombotic response leading to clot formation, and eventually lead to fibrosis, i.e., allow for and stimulate natural cellular ingrowth and proliferation into vascular malformations and the void space of implantable devices located in vascular malformations, such as a cerebral aneurysm, and to stabilize and possibly seal off such vascular abnormalities in a biologically sound, effective and lasting manner.

[00209] In another embodiment of the invention, cellular entities such as fibroblasts and tissues can invade and grow into a reticulated elastomeric matrix. In due course, such ingrowth can extend into the interior pores and interstices of the inserted reticulated elastomeric matrix. Eventually, the elastomeric matrix can become substantially filled with proliferating cellular ingrowth that provides a mass

that can occupy the site or the void spaces in it. The types of tissue ingrowth possible include, but are not limited to, fibrous tissues and endothelial tissues.

[00210] In another embodiment of the invention, the implantable device or device system causes cellular ingrowth and proliferation throughout the site, throughout the site boundary, or through some of the exposed surfaces, thereby sealing the site. Over time, this induced fibrovascular entity resulting from tissue ingrowth can cause the implantable device to be incorporated into the aneurysm wall. Tissue ingrowth can lead to very effective resistance to migration of the implantable device over time. It may also prevent recanalization of the aneurysm. In another embodiment, the tissue ingrowth is scar tissue which can be long-lasting, innocuous and/or mechanically stable. In another embodiment, over the course of time, for example, for from about 2 weeks to about 3 months to about 1 year, implanted reticulated elastomeric matrix becomes completely filled and/or encapsulated by tissue, fibrous tissue, scar tissue or the like.

[00211] The invention has been described herein with regard to its applicability to aneurysms, particularly cerebral aneurysms. It should be appreciated that the features of the implantable device, its functionality, and interaction with an aneurysm cavity, as indicated above, can be useful in treating a number of arteriovenous malformations ("AVM") or other vascular abnormalities. These include AVMs, anomalies of feeding and draining veins, arteriovenous fistulas, e.g., anomalies of large arteriovenous connections, and abdominal aortic aneurysm endograft endoleaks (e.g., inferior mesenteric arteries and lumbar arteries associated with the development of Type II endoleaks in endograft patients). Other embodiments include reticulated, biodurable elastomeric implants for *in vivo* delivery via catheter, endoscope, arthroscope, laparoscope, cystoscope, syringe or other suitable delivery-device and can be satisfactorily implanted or otherwise exposed to living tissue and fluids for extended periods of time, for example, at least 29 days.

[00212] Shaping and sizing can include custom shaping and sizing to match an implantable device to a specific treatment site in a specific patient, as determined by imaging or other techniques known to those in the art. In particular, one or at least two comprise an implantable device system for treating an undesired cavity, for example, a vascular malformation.

[00213] Employment of an implant that can support invasion of fibroblasts and other cells enables the implant to eventually become a biointegrated part of the healed aneurysm. Elastin, fibrin, or other suitable clot-inducing material can also be coated onto the implant providing an additional route of clot formation.

[00214] In one embodiment of the invention the implant can also contain one or more radiopaque markers for visualization by radiography or ultrasound to determine the orientation and location of the implant within the aneurysm sac. Preferably platinum markers are incorporated in the implant and/or relevant positions of delivery members.

[00215] If desired, the outer surfaces of the implant or occlusion device can be coated, after fabrication of the implant or occlusion device with functional agents, such as those described herein, optionally employing an adjuvant that secures the functional agents to the surfaces and to reticulated elastomeric matrix pores adjacent the outer surfaces, where the agents will become quickly available. The functional agents can be coated, during the fabrication of the implant or occlusion device. Such external coatings, which may be distinguished from internal coatings provided within and preferably throughout the pores of reticulated elastomeric matrix used, may comprise fibrin and/or other agents to promote fibroblast growth.

[00216] Once an aneurysm has been identified using suitable imaging technology, such as a magnetic resonance image (MRI), computerized tomography scan (CT Scan), x-ray imaging with contrast material or ultrasound, the surgeon chooses which implant he or she feels would best suit the aneurysm, both in shape and

size. The chosen implant is then loaded into an intravascular catheter in a linear or uncompressed state. The implants can be sold in a sterile package containing a pre-compressed or slightly compressed or uncompressed implant that is loaded into a delivery catheter. Alternatively, the implant can be sold in a sterile package in a linear or uncompressed state, and the surgeon at the site of implantation can use a suitable loading device, e.g. a ring, funnel or chute for loading into the catheter with or without application of compression.

[00217] After an implant according to the invention is loaded into the catheter, the catheter is then advanced through an artery to the diseased portion of the affected artery using any of the techniques known in the art. With use of the catheter the implant of the invention is then inserted and positioned within the aneurysm, the implant filling the aneurysm by bending and folding on itself within the sac. The implant, in an embodiment of the invention, preferably fills the sac conformally, due to inherent properties of the device comprising elastomeric matrix and structural filaments, which properties include properties that allow the device to fold and pack as it fills an aneurysm sac. In another embodiment, the implant according to the invention preferably fills the sac conformally, due to inherent properties of the device comprising viscoelastic and preferably matrix and structural filaments, with properties that allow the device to fold and pack as it fills an aneurysm sac. Properties of the device, in various embodiments, permit the formation of one or more vertices that permit the device to adopt geometries that are non-curvilinear or that otherwise include one or more points at which the device can “break”, fold or otherwise form angles, bends or discretizations, or very small radii of curvature. Properties that permit these sorts of formations, and others according to the present invention, may be conferred by any of a variety of features, including topological features, including but not limited to crimps, the imposition or interaction of additional members or materials, such as filaments, sutures, staples, adhesives, or other additional features or materials without limitation. Embodiments of the device can pack while folding onto itself like in cooked spaghetti, a metallic chain, a thread of honey, or other material capable,

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for example, of adopting sharp direction changes prior to, during, or after introduction into an aneurysm, malformation or other target structure. The device can also pack following a random or irregular curvature or in another case following a more regular curvatures that, for example, resemble helical configurations. The assembly can be enhanced by periodic notches along the length of the assembly forming natural “breaking points,” as well as the platinum (or other) marker band crimping, or other structures as described herein, which further enhances the breaking behavior or other formation of vertices that permit advantageous packing geometries. A non-compressed or slightly compressed linear implant according to the invention will be advanced to conformally fill the aneurysm sac.

[00218] When properly located *in situ*, pursuant to the teachings of this invention, implants or occlusion devices are intended to cause angiographic occlusion of the aneurysm sac. The presence of implants or occlusion devices, optionally including one or more pharmacologic agents borne on each implant, stimulates fibroblast proliferation, growth of scar tissue around the implants, and eventual immobilization of the aneurysm.

[00219] Advantageously, the implants of the invention can, if desired, comprise reticulated biodurable elastomeric implants having a materials chemistry and microstructure as described herein.

[00220] The invention can perhaps be better appreciated from the drawings. In Figure 4, an implant 12 is formed preferably from a biodurable reticulated elastomeric matrix 14 optionally having a regular cross-section such as round, square, ellipsoidal, triangular, rectangular or other multi-sided polygonal cross-sections. In another embodiment, the cross-section of biodurable reticulated elastomeric matrix 14 can be of an irregular shape or random. In yet another embodiment, the cross-section of biodurable reticulated elastomeric matrix 14 can be of regular cross-section for part of the length of implant 12 and can be of irregular cross-section for part of the length of implant 12, that is, a combination of regular cross-section and

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irregular cross-section. In yet another embodiment, the topology of biodurable reticulated elastomeric matrix 14 can be of regular cross-section for part of the length of implant 12 and can be of irregular cross-section for part of the length of implant 12, that is, a combination of regular cross-section and irregular cross-section.

Radiopaque, preferably platinum, markers 16 are positioned or crimped every about 2 to about 10 mm to form a chain link, noodle-like, or other structure consistent with the principles of this and other aspects of the invention.

[00221] In certain embodiments, implant 12 has a structural filament 20 extending through the entire length of implant 12 to prevent implant 12 from jamming, tearing, balling, breaking, or fragmenting, to provide support for pulling and/or pushing during delivery or deployment, and to prevent migration during delivery or deployment. The structural filament, which is attached to the matrix or incorporated into the matrix, comprises preferably a single material such as metal or polymer or in other cases a combination of both. Without being bound by any particular theory, the structural filament provides scaffold or support structure to the implant of the invention, without which the device will tend to buckle during delivery or fold onto itself during storage and handling. This is due to the small cross-sectional area and large length to diameter ratio (or length to any characteristic dimension defining the cross-section) of the implant of the invention whether it is made from reticulated elastomeric matrix or any other viscoelastic thermoplastic or viscoelastic thermoset cross-linked polymeric material. Additionally, the flexibility of the matrix material in most cases without the presence of the structural member will make the device buckle during delivery or fold onto itself during storage, handling, and delivery. The other thermoplastic or thermoset cross-linked polymeric material can be either synthetic or naturally occurring. The need for the structural filament is especially true in the case of materials containing a large amount of voids such as reticulated elastomeric matrix as the inherent mechanical properties of these structures are low due to the presence of high void content and to their inter-connected and inter-communicating open pore structures, features that support tissue ingrowth

and proliferation and eventual bio-integration of the implant to the aneurysm site. Thus the device or devices of this invention while offering sufficient column strength or rigidity or biomechanical integrity for advancement through a catheter or microcatheter, at the same time cannot be too stiff or too rigid so that they are unable to still fold and pack in order to provide a superior packing or filling of the aneurysm on delivery to the aneurysm site.

[00222] Structural filament 20 can be biosorbable or non-resorbable and can comprise a polymer such as polyester, a metal such as platinum, or a combination thereof, including, but not limited to, known suture materials or suture composites. In another embodiment of the invention, the metal can be radiopaque. Moreover, structural filament 20 can be a monofilament fiber, co-mingled fibers, knotted, twisted, braided rope, wire, cable composite scaffold, mesh, woven mesh or knitted mesh. In another embodiment of the invention, filament 20 can be a braided subassembly. In a another embodiment of the invention filament 20 is polymeric fiber, carbon fiber, glass fiber, synthetic polymeric fiber or filament, a single platinum wire, other metallic fiber, a twist or braid of platinum wire and polymeric fiber or filament, or twisted or braided double platinum wires or combinations thereof. In another embodiment filament 20 can be a monofilament. In another embodiment, filament 20 can be a multifilament. In another embodiment, filament 20 can be a reinforcing element. The length of implant 12 could be from about 5 mm to about 800 mm, preferably from about 50 mm to about 600 mm, and the diameter or effective diameter or any dimension or dimensions characteristic of the cross-section could be from about 0.25 mm to about 10 mm, preferably from about 0.50 mm to about 2 mm. In cases where the structural filament 20 can be biosorbable, as the structural filament degrades over time, it may make more of the cross-section accessible to tissue ingrowth and proliferation.

[00223] A matrix according to the present invention, such as the polymeric matrix, which is biodurable, elastomeric, and reticulated, together with the one or more structural filaments embedded in or incorporated into the matrix, forms an embodiment of the implant of the invention. This structure has a number of advantages when it is used to fill an irregularly shaped aneurysm sac. In certain embodiments, the presence of the one or more structural filaments, when imbedded or incorporated in the matrix, enhances the propensity of the implant to form coil-like shapes that allows it to pack in an easier fashion and fill the aneurysm and in the process allows the implant to conformally fill the sac in a way that conforms in a superior fashion to the internal shape and volume of the sac. In other embodiments of the invention, the presence of the one or more structural filaments, when imbedded or incorporated into the matrix, enhances the propensity of the implant to fold onto itself like spaghetti, chain, a thread of honey or the like, and allows it to pack and fill the aneurysm, in the process allowing the implant to conformally fill the sac in a way that conforms in a superior fashion to the internal shape and volume of the sac. In another embodiment, the device can pack while folding onto itself like such that the deposition of the material in the manner of a piece of cooked spaghetti to form a string ball in the aneurysm. The device can pack following random or irregular curvatures or in another case following more regular curvatures that, for example, resemble helical configurations. In embodiments of the invention, as also described above, the presence of the one or more material, topological or other features or structures, such as structural filaments, when imposed, imbedded or incorporated in the matrix, create or enhance a propensity of the implant to form vertices, such as folds, angles, discretized, or non-curvilinear geometrics, or very low radii of curvature, and to also form shapes containing curvatures allowing the implant to conformally fill the sac in a way that conforms in a superior fashion to the internal shape and volume of the sac. In certain embodiments, implants or devices according to this aspect of the present invention can be applied in actual or virtual layers, being deposited in a manner akin to strokes of a paintbrush or other suitable insertion or deposition techniques.

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Implants or devices that have a propensity to form shapes containing curvatures and/or those that fold onto itself optionally can be compressed as they make contact during delivery with other parts of itself or with other delivered devices in the aneurysm or with wall of the aneurysm thereby making it easier to pack in a superior fashion. This progressive compression of the device allows for superior packing, as the device is able to fill small regions of the previously unfilled aneurysm sac. This is better appreciated when the use and availability of different soft and ultra soft devices, that facilitates and enhances this superior packing towards the end of the procedure of implanatation, and will be presented and discussed below. The device, or portions of it, may in certain embodiments, including but not limited to generally stringlike or other elongate forms, be formed in order to otherwise lack a predetermined shape or geometry in order to enhance its conformal filling behavior and resultant superior packing density.

[00224] The presence of the one or more structural filaments also prevents jamming, tearing, balling, breaking, or fragmenting, to provide support for pulling and/or pushing during delivery or deployment, and to prevent migration during delivery or deployment. Without being bound by any particular theory, the absolute or comparative stiffness of the structural members in relation to the matrix in certain embodiments allows these additional advantages. It is believed that additional periodic material or topological features, including but not limited to crimps or notches along the length of the implant, or shapes, couplings, or other relationships between components of the device that can be formed along its length, as described above, permit the member to be modulated, inserted, and/or deposited in a conformal or other desired geometry with respect to the target structure. In one embodiment, such feature(s) may the optionally add other features, such as making the device radiopaque in certain embodiments by crimping platinum or other marker bands along the length of the device to form a structure that also preferably forms vertices (as described above) or otherwise folds at or around these periodic notches and/or crimped platinum marker bands allowing the implant to fill the sac in a way that

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conforms in a superior fashion to the internal shape and volume of the sac. The overall resultant phenomenon is again similar to that of cooked spaghetti filling a bowl, for example, and the folded spaghetti-like structure of an embodiment of the implant of the invention provides more complete packing of the aneurysm sac when compared to platinum coils or other polymeric devices that are pre-formed or imparted with a shape prior to delivery to the aneurysm sac. The resulting packing is more complete or tight and is much less likely to have voids or unfilled space when compared to platinum coils or other polymeric devices that are pre-formed or imparted with a shape prior to delivery to the aneurysm sac. In certain embodiments of this invention the column strength or rigidity or biomechanical integrity device or devices of this invention can be engineered and controlled to facilitate delivery for their advancement through a tortuous catheter or microcatheter and at the same time not make the devices too stiff or too rigid so that they are unable to still fold and pack in order to provide a superior packing or filling of the aneurysm on delivery to the aneurysm site.

[00225] In another embodiment, the implant can have a predetermined shape which the implant would assume at least substantially the predetermined shape upon deployment from the delivery system. In another embodiment, the implant with a predetermined shape would assume shape similar or equivalent to the predetermined shape upon deployment from the delivery system. The preset shape or memory comprises both configuration and dimensions. Examples of preset shapes include, but are not limited to, helical, spherical, conical, etc. The dimensions of such preset shapes would be determined by the outer diameter of the loops or the largest other maximum dimension, and for example, could range from about 2 mm to about 20 mm. Implants with predetermined shapes are particularly advantageous when used as “framing” strings to line the interior circumference of the aneurysm and thereby prevent migration of “filling” strings out of the neck of the aneurysm during subsequent packing.

[00226] The implant 22 in Figure 5 comprises two or more, preferably from about 3 to 6, cylindrical or string segments 24 that are held together by a structural filament (not shown) or marker 26 for structural integrity for delivery or deployment or to be blended with other components. As with implant 12, radiopaque markers 26 are crimped from about 2 to about 10 mm apart. The length and effective diameter of implant 22 are approximately the same as those of implant 12.

[00227] Another embodiment of an implant 30, also known as a NEURO-STRING™ implant, is shown in Figures 6 to 9. Implant 30 is formed from an elastomeric matrix member 32 having a round, square, ellipsoidal, multi-sided, polygonal, or rectangular, but preferably round, cross-section. In another embodiment, implant 30 is formed from an elastomeric matrix member 32 having an irregular shape. In yet another embodiment, the cross-section of elastomeric matrix 32 can be of regular cross-section for part of the length of implant 30 and can be of irregular cross-section for part of the length of implant 30, that is, a combination of regular cross-section and irregular cross-section. In yet another embodiment, the topology of biodurable reticulated elastomeric matrix 32 can be of regular cross-section for part of the length of implant 30 and can be of irregular cross-section for part of the length of implant 30, that is, a combination of regular cross-section and irregular cross-section. In another embodiment, matrix member 32 is biodurable and reticulated. Two longitudinally extending, essentially parallel structural filaments 34 and 36 extend the length of implant 30, and at regular intervals structural filaments 34 and 36 form knots or ropes 38 that define matrix subsections 40. A purpose of the knots is to secure the structural filament to the elastomeric matrix. This can be seen more clearly in the detail of Figure 7. Other means of incorporating filaments 34 and 36 into matrix 32 that causes similar attachment are commonly known, for example, sewing stitches. The respective ends of structural filaments 34 and 36 form a loop 42 at the proximal end 44 and optionally also distal end 46, of implant 30.

[00228] Structural filaments 34 and 36 can be biosorbable or non-resorbable,

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preferably non-resorbable, and comprised of a polymer such as polyester, a radiopaque metal such as platinum, or a combination thereof, including, but not limited to, known polymeric fiber or filament materials or polymeric fiber or filament composites. Moreover, reinforcing filaments 34 and 36 can each be a monofilament, braided rope or wire, or a wire or cable.

[00229] In an embodiment of the invention, one or more elongate structural members in the device, such as filaments, may be included and, if so, may be provided with features or coupled to one another to confer desired properties. Filament 34 may be polymeric fiber, carbon fiber, glass fiber, synthetic suture, a single platinum wire, other metallic fiber, a twist or braid of platinum wire and polymeric fiber or filament, or twisted or braided double platinum wires or other materials or combinations thereof. Filament 36 is polymeric fiber or other filament such as are described above. Filament 34 or filament 20 can also be a monofilament fiber, co-mingled fibers, knotted, twisted braided rope, wire, a cable, composite scaffold, mesh, woven mesh or knitted mesh, or other material, structure or combination. In one embodiment according to the invention, filament 34 can be a structural element. Filament 34 may comprise a sub-assembly prepared using a coil winder and separate spools of fibers used to make polymeric fibers or filaments and platinum wires of differing thicknesses, thereby creating a twisted rope-like composite subassembly with varying stiffness and radiopacity. Known methods such as braiding may also be used to create such a subassembly. In another embodiment of the invention, the components of filament 34 may be available on separate spools or spindles and the final structural element can be formed during the attachment or the incorporation of the matrix member 32 to filament 34. In another embodiment, filament 34 may comprise a sub-assembly in which a platinum micro coil string wound from platinum micro wire, over a fiber core or over the platinum wire core, will provide more integrity for pull/push action including good radiopacity. Construction or fabrication of filament 34 can be achieved in, for example, by using a sewing machine. Instead of using twisted platinum wire with fiber into braid and than loaded into sawing machine, in one

embodiment a regular coil having inner core fiber or platinum wire is then loaded into the sewing machine to get knotted with the second sewing machine polymeric fiber or filament or wire string.

[00230] The platinum wire useful according to the invention preferably has a diameter of from about 0.0005 in. to about 0.005 in., more preferably from about 0.001 in. to about 0.003 in. Suitable platinum wire is available from sources such as Sigmund Cohn Corp. The fibers useful according to the invention comprise commercially available, non-absorbable polymeric fibers used to make suture fiber or filament having an effective diameter of from about 0.0005 in. to about 0.010 in., preferably from about 0.010 in. to about 0.005 in. Preferably the fibers are available on spools and have compositions and diameters comparable to commercially available sutures, for example, sutures available from Johnson & Johnson under the name ETHIBOND EXCEL®, PROLENE®, ETHILON®, Coated VICRYL®, or MONOCRYL®.

[00231] Varying the structural filaments results in implants according to the invention having different characteristics. When each of the filaments is polymeric fiber or filament, the resulting implant is "Ultra Soft", as set forth in the table below. When at least one of the filaments includes platinum wire, the resulting implant is "Soft" or "Stiff". The stiffness of the device can be measured by the slope of the load versus extension curves during an uniaxial tensile pull using a tensile testing machine and can be in the range of from 1 to 200 pounds per inch (0.18 N/mm to 35 N/mm), preferably in the range of from 5 to 100 pounds per inch (0.88 N/mm to 18 N/mm). The breaking strength of the device can be measured during an uniaxial tensile pull using a tensile testing machine and can be in the range of from approximately 0.05 to 23 pounds (0.2 to 100 Newtons) and preferably in the range of approximately 0.05 to 7 pounds (1.0 to 30 Newtons).

Table 1.

Filament 204 (bottom bobbin)	Filament 206 (top bobbin)	Resulting Implant stiffness & functionality
Fiber equivalent to (7-0) Suture with approx. diameter = 0.05 mm	Fiber equivalent to (7-0) suture with approx. diameter = 0.05 mm	"Ultra Soft" implant for finishing (filling residual gaps in aneurysm), requires core wire/coaxial pusher or hydraulic assistance for delivery.
Single Pt wire (0.002-0.005")	Fiber equivalent to (7-0) suture with approx. diameter = 0.05 mm	"Soft" implant for framing and filling the aneurysm, can be pushed from proximal end using a pusher member.
Twisted or braided Pt wire + Fiber equivalent to (7-0) Suture with approx. diameter = 0.05 mm	Fiber equivalent to (7-0) suture with approx. diameter = 0.05 mm	
Twisted or braided Double Pt wire	Fiber equivalent to (7-0) suture with approx. diameter = 0.05 mm	"Stiff" implant for framing the aneurysm, can be pushed from proximal end using a pusher member.

[00232] It is preferred to include additional platinum markers to be crimped in from 1 to 10 mm sequences to provide safe radiopacity/visibility. Framing coils or a stent may be used to prevent migration. Delivery of the Ultra Soft implant requires use of the supporting core-wire delivery system described below in Figure 22 or hydraulic injection with a syringe. Delivery of the Soft or Stiff implants requires a pusher member as described below in Figures 16, 17, and 18.

[00233] When according to the invention one structural filament is a platinum wire and the other structural filament is polymeric fiber or filament, the resulting implant behaves like a coil to form helical packing during deployment into the aneurysm sac. A significant difference between an implant of the invention and a coil is that the implant of the invention does not have a predetermined memory, as does a coil. Also, the implant of the invention is malleable and will conform to the dimensions of the aneurysm sac. The stiffness can be controlled by varying the diameter of the platinum wire or the structure, as shown above, and the filament

structure can act as a framing structure in lieu of the framing coils or stent necessary with a softer implant. The stiffness can also be controlled by varying the number of platinum wires used. The stiffer implants function to prevent migration and to facilitate better packing of the aneurysm sac, while the softer versions can be used as filler material to optimally embolize the aneurysm. This stiffer implant may be more useful for different vessel occlusion applications within the body. Delivery of the stiffer implant can be accomplished with a regular delivery system not having a supporting core-wire mandrel or hydraulic injection.

[00234] It is within the scope of the invention that each filament can be a platinum wire. The resulting implant will be similar to the implant described above but slightly stiffer and more radiopaque.

[00235] In an embodiment of the invention implant 30 has regularly spaced radiopaque markers that are attached to every second to every sixth knot, preferably every third or fourth knot. These radiopaque markers tend to encourage the chain-like behavior that is characteristic of this embodiment. Notching of the elastomeric matrix/structural assembly and optional periodic crimping of platinum marker bands will allow the implant of the invention to bend and fold when deployed in an aneurysm and break like a chain. This bending and folding allows the implant to conformally fill the aneurysm sac like a liquid when deployed from the microcatheter. The overall resultant phenomenon is again similar to that of spaghetti filling a bowl or a metallic chain folding onto itself. In certain cases the implant fills the aneurysm sac in a manner similar to that of very viscous liquid flow. When multiple implants are placed in an aneurysm, the implants or devices form shapes containing curvatures or those that fold onto themselves optionally can be compressed further as they make contact during delivery with themselves or with other delivered devices in the aneurysm or with wall of the aneurysm, thereby making it easier to pack in a superior fashion. Platinum marker bands will impart additional radiopacity.

[00236] In another embodiment of the invention radiopaque microstaples instead of the radiopaque markers could be regularly spaced along the length of the implant every second to every sixth knot. This configuration would also encourage chain-like behavior.

[00237] In another embodiment of the invention which is shown in detail in Figure 8, an implant 50 has filaments 52 and 54 similar to the structure described above but with an additional filament 58. Filament 58 comprises platinum wire or polymeric fiber or filament and provides additional structural integrity. Optionally implant 50 may have loops 60 attached to every fourth to twentieth knot 62. Loops 60 comprise polymeric fiber or filament or physiologically acceptable, optionally radiopaque, metal such as platinum wire. Loops 60 are used to attach Ultra Soft implants according to the invention to the core wire/coaxial pusher during delivery.

[00238] In the embodiment of the invention shown in Figure 9, an implant 66 has proximal and/or distal, preferably radiopaque, coils 68. Coils 68 preferably are non-linear in an unstressed state. For example, when an implant having such coils is advanced into an aneurysm, the coils, especially the distal coil, will assist in conformally filling the aneurysm. The distal coil, that is, the first coil out of the microcatheter, functions to start the implant breaking in the aneurysm sac. When this coil hits the wall, it curls on itself into a half-loop, which initiates the breaking behavior of the implant which follows. The proximal coil, that is, the last coil out of the microcatheter before detachment, serves as a visual "end point" to the operator that he/she has deployed the end of the implant. This is advantageous in providing a clear "start" & "stop" visual marker system which other implants don't have.

[00239] The length of implant 30 or 50 could be from about 5 mm to about 1500 mm, preferably from about 1 cm to about 50 cm, and the diameter or effective diameter could be from about 0.25 mm to about 12 mm, preferably from about 0.250 mm to about 0.5 mm. The defined sections of the implant are each from about 0.5 mm to about 1 cm in length. The implant of the invention is delivered in an

uncompressed state. Also, the reticulated elastomeric matrix and the structural filaments are intertwined or the latter is incorporated into the former so that they, in effect, work together, more notably that the structural filaments provide support to the elastomeric matrix. There should be at least from about 1 to about 4 pores of reticulated elastomeric matrix material surrounding the structural filaments, even after trimming or shaving the elastomeric matrix material as described below. In another embodiment, there should be at least from about 1 to about 10 pores of reticulated elastomeric matrix material surrounding the structural filaments, even after trimming or shaving the elastomeric matrix material as described below.

[00240] During the shaving or trimming some of the pores may open to form concavities, that is, any structure having at least one concave surface feature, that may or may not be fully contained within the implant or may intersect an outer surface of the implant, which may have a dimension greater than the maximum diameter of the implant, and which may encompass pores, partial or fragmentary pores, cavities that alone, or combined to form "virtual" pores, accommodate tissue ingrowth. Such structure also encompasses honeycomb structures, which may comprise a plurality of fully and/or partially contained concavities in the form of pores, and a skeleton or framework of a reticulated foam, in which the concave partial surfaces remain or are formed after an implant is shaved or trimmed to its final or operative width.

[00241] The number of pores present after shaving or trimming may inversely correlate to the pore size of the material in that there will be a greater number of pores remaining in material with a smaller pore size. When deployed in the aneurysm, the implant of the invention bends and folds (plicates), creating a conformal "foam ball" that serves as a porous scaffold for tissue ingrowth. Even though each individual string may only have 4 to 5 pores, optionally from 2 to 10 pores, the plication of the implant allows creation of a "solid" conformal scaffold.

[00242] According to the invention the structural filaments can be inserted into an elastomeric matrix by hand or by mechanical means such as a mechanical stitching

or sewing machine. Preferably a commercial sewing machine having two bobbins is used where each bobbin has filament material. In a preferred embodiment one bobbin has a braided platinum wire/polymeric fiber or filament filament subassembly and a second bobbin has polymeric fiber or filament. These subassemblies are then sewn into elastomeric matrix sheet material of from about 1 to about 2 mm thickness to create a continuous stitch line from about 10 to about 50 cm long. In another embodiment of the invention, an adhesive can be used to adhere a single structural filament to the elastomeric matrix, such as by dipping or polymerizing the adhesive to the structural filament. The elastomeric matrix is then carefully trimmed or shaved by hand to a desired diameter. The outer diameter of each elastomeric matrix section should be equal to or slightly less than the inner diameter of the corresponding introducer sheath, discussed below.

[00243] In a preferred embodiment of the invention set forth in Figures 10A to 10C, longitudinally extending platinum coils 80 are positioned axially or longitudinally along extended polymer filament or fiber 82 to form sub-assembly 84. Polymer filament or fiber 82 is also known as structural filament. Coils 80 are from about 0.010 in. to about 0.250 in. in length and have an o.d. of from about 0.003 in. to about 0.050 in. The coils 80, which have an i.d. of from about 0.001 in. to about 0.004 in., are positioned along filament 82 with space of from about 0.005 in. to about 0.100 in. inbetween. Coils 80 can optionally be comprised of a radiopaque or substantially radiopaque metal or alloy other than platinum, such as nitinol or titanium. Also, each coil 80 may vary in size or material. Filament or fiber 82 may be comprised as described otherwise herein for filaments or fibers, including, but not limited to, the composition and/or structure of filament 34 or 36.

[00244] To assemble the embodiment of Figures 10A to 10C, coils 80 are prepared from a longer coil (not shown) and then threaded onto filament 82 in "necklace-like" fashion. The outer diameter of filament 82 and the inner diameter of each coil 80 are sufficiently close that coils 80 maintain desired position on filament

82. Optionally a physiologically acceptable glue or crimping could be used to maintain spacing of coils 80 on filament 82. Alternatively, coils 80 could be attached or affixed to filament 82 by other manual, mechanized, or automated procedures that would be appreciated by one skilled in the art. Filament 82 can be a monofilament fiber, co-mingled fibers, knotted, twisted, braided rope, wire, cable composite scaffold, mesh, woven mesh or knitted mesh. In another embodiment of the invention, filament 82 can be a braided subassembly. In another embodiment of the invention filament 82 is polymeric fiber, carbon fiber, glass fiber, synthetic polymeric fiber or filament, a single platinum wire, other metallic fiber, a twist or braid of platinum wire and polymeric fiber or filament, or twisted or braided double platinum wires or combinations thereof. In another embodiment filament 82 can be a monofilament. In another embodiment, filament 82 can be a multifilament. In another embodiment, filament 82 can be a reinforcing element.

[00245] Sub-assembly 84 of Figure 10A is then inserted into longitudinally extending elastomeric matrix 88, by use of a sawing needle. Elastomeric matrix 88 is cut, for example, with a micro scissors, to attain a desired diameter and to form the elongated structure 92 shown in Figure 10C.

[00246] Optionally, and preferably, an external fiber or filament 96 is wound diagonally on the outer surface 98 of elastomeric matrix 88, to secure or attach elastomeric matrix 88 to sub-assembly 84. Filament 96 may comprise a polymeric fiber as described herein or, to increase radiopacity, a radiopaque material such as or platinum or nitinol.

[00247] In a variation of the embodiment described above, with or without external filament 96, elastomeric matrix 88 may adhere to sub-assembly 84 due to thermal treatment, crimping, or a physiologically acceptable glue.

[00248] The structure of sub-assembly 84 is important with regard to implant flexibility, which can be varied by adjusting the spacing of coils 80 on filament 82.

Large gaps between coils 82 result in a more flexible implant, whereas smaller gaps would result in a less flexible implant.

[00249] In a sub-assembly 100 shown in Figure 11, platinum bands or hypo-tube segments 102 are positioned on a fiber or filament 104, similar to the arrangement shown in Figure 10A. The dimensions and materials are the same as in sub-assembly 84, with the use of hypo-tube segments 102 rather than coils 80 and filament 104 being similar to filament 82. Similarly, in the sub-assembly 106 shown in Figure 12, coils 108 and hypo-tube segments 110 are alternatingly positioned on fiber or filament 114. It is within the scope of the invention that the order and relative numbers of coils 108 and hypo-tube segments 110 can be varied. And then, in the preferred sub-assembly 120 shown in Figure 13, a fiber or filament 120 extends through a lumen (not shown) of a longitudinally extending radiopaque coil 122. Coil 120 will have the same cross-sectional parameters as coil 80 or 108, and it will have a length of from about 0.5 cm to about 50 cm.

[00250] Sub-assembly 100, 106, or 120 can then each be inserted into a longitudinally extending elastomeric matrix (not shown), as was sub-assembly 84 of Figures 10A to 10C.

[00251] In one embodiment of the invention, a hypo-tube segment such as hypo-tube segment 102 or 108 may have slots or perforations, which has the advantage of imparting or increasing flexibility. Although not bound by any particular theory, it is expected that such a hypo-tube segment would not stretch in the same manner and extent as a coil might, and the higher stretching of a coil might be disadvantageous in some applications. A detail of hypo-tube segment 102 is shown in Figure 14, where alternating slots 124 have been cut, preferably with a laser, into a wall 126 of hypo-tube segment 102. Each hypo-tube segment is from about 0.010 in. to about 0.250 in., preferably from about 0.025 in. to about 0.150 in., in length and has an i.d. of from about 0.002 in. to about 0.006 in., preferably from about 0.003 in. to about 0.005 in., and an o.d. of from about 0.004 in. to about 0.008 in., preferably from about 0.005 in.

to about 0.007 in. The depth 128 of each slot 124 is from about 0.002 in. to about 0.006 in., preferably from about 0.003 in. to about 0.005 in., and the initial cutting width 130 is from about 0.0005 in. to about 0.0025 in., preferably from about 0.001 to about 0.002 in. The spacing 132 between slots 124 is from about 0.001 in. to about 0.005 in., preferably from about 0.002 in. to about 0.004 in.

[00252] In the embodiment of the invention shown in Figures 15A to 15C, a braid 134 comprises a multitude of individual fiber or filaments, for example, from about 2 to about 20, preferably from about 4 to about 16. The filaments can be selected from the group consisting of polymeric fiber, carbon fiber, glass fiber, synthetic suture, a single platinum wire, nitinol wires or ribbons other metallic fiber, a twist or braid of platinum wire and polymeric fiber or filament, or twisted or braided double platinum wires or other materials or combinations thereof. Braid 134 is inserted into elastomeric matrix 136 using a needle machine, and optionally, a polymeric or platinum filament or wire 138 can be diagonally wound around the external surface 140 of elastomeric matrix 136.

[00253] According to the invention, the structural filaments can be inserted into thin sheets of an elastomeric matrix sheet material of from about 1 mm to about 3 mm thickness by using a needle to longitudinally draw the structural filaments into the sheet. After being pulled into the elastomeric matrix, the matrix can be cut to the required implant length and then carefully trimmed or shaved by hand to a desired diameter, forming an initial elongated structure. Optionally, an external polymeric filament can be loosely wrapped on a diagonal bias to secure elastomeric matrix to the subassembly. Several known material processing treatments that use mechanical deformation with and without thermal energy or heat treatment can then be utilized to adhere the elastomeric matrix to the subassembly and also to downsize the cross-section area, or cross-section diameter or maximum cross-section dimensions of the initial elongated structure to the final target diameter such that the outer diameter of the elastomeric matrix should be equal to or slightly less than the inner diameter of the

corresponding introducer sheath, discussed below.

[00254] A system 146 for the delivery of a Soft or Stiff implant according to the invention such as implant 30 or other implants according to the invention is shown in Figure 16. Proximal end 142 of implant 30 is engaged within an introducer sheath 148 by the distal end 150 of a pusher rod or member 152. The proximal end 154 of sheath 148 engages the distal portion 156 of a manifold or side arm 158, which has an opening 160 for continuous flush. Pusher member 152 extends proximally through valve 162, and pusher member 152 has a lumen (not shown) which receives an interlocking wire 164, which provides support to pusher member 152 and helps retain implant 30.

[00255] For delivery of implant 30 or another occlusion device according to the invention to a patient, a flushing solution such as saline solution is introduced into opening 160 of system 146 to remove air and straighten out implant 30. Then, the tapered distal tip 166 of sheath 148 is introduced with continuous flushing into the hemostatis valve 168 of a side arm 170 of a microcatheter assembly 172 such as is shown in Figure 17. Sheath 148 is inserted into microcatheter 174, after which sheath 148 and side arm 170 are withdrawn, leaving implant 30, pusher member 152, and interlocking wire 164.

[00256] Delivery of implant 30 is shown in Figures 17 and 18, where the distal end 144 of implant 30 is advanced through microcatheter 174 and through an artery 176 to a position adjacent an aneurysm 178. Implant 30 is advanced further to fill aneurysm 178. When aneurysm 178 has been filled, as shown in Figure 18, the distal end 150 of pusher rod 152 is disengaged from implant 30 and withdrawn through microcatheter 174.

[00257] In another embodiment of the invention shown in Figures 19 to 20, the delivery of an expandable implant according to the invention is shown. An elastomeric structure 180 comprises two or more sections 182, preferably from about

2 to about 100, that are defined by radiopaque rings, e.g., platinum rings or compression members 184 or similar mechanisms. Elastomeric sections 182 comprise a longitudinally extending flexible mesh 188 defining a lumen 192. A distal spring section 194 attached to the distal end 196 of structure 180 comprises a distal tip 198 and a lumen 200 in communication with lumen 192. At the proximal end 204 of structure 180 a proximal spring 202 is attached to proximal end 204 and has a lumen 206 extending therethrough. A flexible but rigid wire 208 extends through lumen 206, lumen 192, and lumen 200. Wire 208 has a radiopaque tip marker 190. Flexible mesh 188 extends distally as a jacket to cover coil 194 and proximally as a jacket to cover coil 202.

[00258] Compressed structure 180 is positioned within a delivery catheter 210 that has a longitudinally extending lumen 212 and a distal radiopaque marker 216. The proximal end 218 of catheter 210 has a narrowed opening 220 that slidably engages a pushing catheter 224.

[00259] The proximal end 226 of pushing catheter 224 slidably engages the proximal section 228 of wire 208. The distal end 232 of pushing catheter 224 comprises a radiopaque marker 234 and an opening 236. A flexible loop or wire 238 attached to coil 206 extends through opening 236 to engage wire 208.

[00260] To deploy structure 180, as shown in Figure 20, pusher catheter 224 and wire 208 are advanced distally. As portions of structure 180 extend distally past the distal end 240 of delivery catheter 210, wire 208 is withdrawn in the proximal direction. Eventually, as shown in Figure 21, wire 208 is withdrawn past opening 236 so that flexible wire 238 releases and structure 180 is free from delivery catheter 210.

[00261] Preferably coils 200 and 206 and mesh 188 comprise a biocompatible shape memory alloy or polymer such as nitinol, so that the released structure will assume a non-linear, preferably helical or irregular, shape.

[00262] It should be appreciated that in the aspect of the invention shown in Figure 20 the implant is still connected to the delivery “system” via connecting member 238. This is important because the implant can in this partially delivered condition be maneuvered within the patient to either reposition the implant to optimize placement allowing for a controlled delivery, or even to withdraw or retrieve the implant altogether.

[00263] In the delivery system shown in Figure 22 the delivery of an Ultra Soft implant according to the invention is shown. Implant 250 comprises filaments 252 and 254 that form knots 256. Implant 250 has a distal section 260 that comprises a preferably radiopaque coil with helical memory 262 having a proximal washer 264. A proximal section 266 of implant 250 comprises a preferably radiopaque coil with helical memory 268.

[00264] Implant 250 is positioned coaxially within a catheter 270, preferably a microcatheter for cranial access and embolism. A pusher sheath 272 has a distal portion 276 with an opening 278. Filaments 252 and 254 form a loop 280 that extends through coil 268 and opening 278 to engage a core wire or mandrel 284. Core wire 284 has a radiopaque distal tip 286. Knots 256 have regularly spaced loops 290 that engage core wire 284.

[00265] Core wire 284 has two functions: First, core wire 284 is to provide support to the implant 250 during distal advancement to prevent buckling, due to the nature of the soft material. Core wire 284 distal tip 286 is compressed against distal washer 264 to keep implant 250 at the required tension during distal advancement to the distal part of catheter 270.

[00266] Once the distal tip 260 of implant 250 is advanced to the distal tip of catheter 270, core wire 284 is retracted back into coaxial pusher sheath 272 for a few centimeters, for example, from about 2 to about 5 cm., and the core wire 284/sheath 272 assembly is then used to push only implant 250 out of catheter 270 and into an

aneurysm (not shown). For implants longer than 5 cm, this process is repeated until the entire length of implant 250 is delivered to the aneurysm. Core wire 284 must always remain within the catheter and be gradually retracted back into the pusher sheath 272 until the entire implant 250 is out of catheter 270 and ready for controlled detachment.

[00267] Controlled detachment is the second function of core wire 284. When implant 250 is ready to be detached, core wire 284 is retracted proximally to the extent of opening 278 to release loop 280, whereby implant 250 will separate instantly from the delivery system.

[00268] The purpose of proximal coil 268 and distal coil 262 is to provide safe/soft beginning and end of implant deployment into delicate vasculature of the aneurysm wall. The coils preferably have a helical memory, at least one 360° loop, to start folding the implant, as compared to straight penetration deployment. Also, the coils provide excellent radiopaque visibility during initial placement to anchor the implant within the aneurysm sac to prevent migration, by selecting optimal shape memory diameter of the coils to anchor within the diameter of the sac. The coil loop diameter must be larger than the neck/opening of the aneurysm to prevent migration.

[00269] A detail of the connection between the proximal end 302 of implant 30 and the distal end member 304 of pusher member 306 is shown in Figures 23 and 24 and describes the suture loop mechanical detachment system used to detach the different implants according to the invention, including Ultra Soft, Soft, and Stiff implants. Distal end member 304 comprises a lateral opening 310 to receive loop 312 from implant 30 and threading 316. The distal end 318 of wire 320 has reciprocal threads 322 that engage threading 316. In the position shown in Figure 23, the distal end 318 of wire 320 is adjacent to the internal end surface 326 of distal end member 304, to trap loop 312. When wire 320 is rotated to cause wire 320 and threads 322 to disengage from threading 316, loop 312 disengages from wire 320 and pusher member 306 and releases implant 30. Also, preferably distal end member 304

comprises radiopaque material such as platinum to assist an operator during delivery. For example, distal end member 304 could comprise a section of platinum hypo-tube. More preferably, the distal end 318 of wire 320 is also radiopaque, which assists the operator during the procedure. When distal end member 304 and distal end 318 are engaged, there will be a single spot under fluoroscopy; however, when distal end member 304 and distal end 318 disengage and release the loop from the implant, there will then be two separate spots under fluoroscopy to signify that release.

[00270] Advancing through microcatheter 174 provides controlled delivery or retraction of implant 30 into the aneurysm cavity with the pusher member 152 until desired positioning of implant 30 is accomplished. Due to the nature of the implant material, the implant fills the aneurysm cavity like a liquid complying with the geometry of the cavity. Continuous flush or pump of hydraulically pressurized solution such as saline solution is applied via microcatheter through the microcatheter side arm at the proximal end to support or drive the advancement of the implant through the catheter lumen. Dependent upon the size of the aneurysm, single or multiple implants may be necessary to achieve total occlusion. The packing density, that is, the ratio of volume of embolic material to volume of the aneurysm sac, ranges from at least about 10% to at least about 200%. Implant 30 can be retracted, before it is detached, and repositioned for precise, controlled deployment and delivery.

[00271] Implant 30 is not self-supporting and has no predetermined shape. It conforms significantly better to the geometry of the aneurysm than other implants due to the formation of a light, non-traumatic member filling the cavity like a fluid such as a highly viscous liquid. Because of this important feature the implant material will provide permanent stability of the desired total occlusion. An additional important feature of implant 30 is that it provides excellent tissue ingrowth to seal the aneurysm cavity from the parental artery. There is superior tissue ingrowth due to the porous nature of the reticulated matrix enhanced by structural reticulation created by plication/folding within the aneurysm. Also, plication enhances conformal space

filling that eliminates device compaction and recanalization.

[00272] Some materials suitable for fabrication of the implants according to the invention will now be described. Implants useful in this invention or a suitable hydrophobic scaffold comprise a reticulated or substantially reticulated polymeric matrix formed of a biodurable polymer that is elastomeric. In one embodiment, polymeric matrix formed of a biodurable polymer is resiliently-compressible so as to regain its shape after being subjected to any compression during delivery to a biological site such as vascular malformations described here. The structure, morphology and properties of the elastomeric matrices of this invention can be engineered or tailored over a wide range of performance by varying the starting materials and/or the processing conditions for different functional or therapeutic uses.

[00273] The inventive implantable device is reticulated, i.e., comprises an interconnected network of pores and channels and voids that provides fluid permeability throughout the implantable device and permits cellular and tissue ingrowth and proliferation into the interior of the implantable device. The inventive implantable device is reticulated, i.e., comprises an interconnected and/or intercommunicating network of pores and channels and voids that provides fluid permeability throughout the implantable device and permits cellular and tissue ingrowth and proliferation into the interior of the implantable device. The inventive implantable device is reticulated, i.e., comprises an interconnected and/or intercommunicating network of pores and/or voids and/or channels that provides fluid permeability throughout the implantable device and permits cellular and tissue ingrowth and proliferation into the interior of the implantable device. The biodurable elastomeric matrix or material is considered to be reticulated because its microstructure or the interior structure comprises inter-connected and intercommunicating pores and/or voids bounded by configuration of the struts and intersections that constitute the solid structure. The continuous interconnected void phase is the principle feature of a reticulated structure.

[00274] Preferred scaffold materials for the implants have a reticulated structure with sufficient and required liquid permeability and thus selected to permit blood, or other appropriate bodily fluid, and cells and tissues to access interior surfaces of the implants. This happens due to the presence of inter-connected and inter-communicating, reticulated open pores and/or voids and/or channels that form fluid passageways or fluid permeability providing fluid access all through.

[00275] In another embodiment the inventive implantable device is only partially reticulated. Thus it contains some segments that are reticulated, i.e., comprises an interconnected network of pores and channels and voids that provides fluid permeability throughout the implantable device and permits cellular and tissue ingrowth and proliferation into the interior of the implantable device. However, it also contains sections that are not reticulated. The inventive implantable device, in another embodiment is partially reticulated, i.e., comprises segments that are interconnected and/or inter-communicating network of pores and channels and voids that provides fluid permeability throughout the implantable device and permits cellular and tissue ingrowth and proliferation into the interior of the implantable device. In this case, one reticulated segment may be separated from another reticulated segment by sections of unreticulated segments.

[00276] In another embodiment the inventive implantable device is not necessarily reticulated. It may or may not contain pores and channels and voids. It may or may not contain pores and channels and voids that are interconnected and/or inter-communicating. However, after the device is delivered and the device fills the sac in a way that conforms substantially to the internal shape and volume of the sac, the spaces between the different segments of the device can form at least a partially interconnected and partially inter-communicating space or passage created by plication/folding of the device within the aneurysm. These partially interconnected and partially inter-communicating space or passage can also be created by a single device or by crossing or intersections of multiple devices. This partially

interconnected and partially inter-communicating space or passage, can be termed as structural reticulation, and provides fluid permeability throughout the implantable device and permits cellular and tissue ingrowth and proliferation into the interior of the implantable device. In general polymeric matrix, which is preferably biodurable, elastomeric, and reticulated, together with the one or more structural filaments embedded in or incorporated into the matrix, forms an embodiment of the implant of the present invention. However, in the case discussed in this embodiment involving an implantable device or matrix that is not necessarily reticulated, may or may not contain pores and channels and voids and may or may not contain pores and channels and voids that are interconnected and/or inter-communicating, the present invention also teaches that one or more structural filaments need not be embedded in or incorporated into the matrix. It is important to note that in accordance with one of the preferred embodiments of this invention, the column strength or rigidity or biomechanical integrity device or devices of this invention can still be engineered and controlled to facilitate delivery for their advancement through a tortuous catheter or microcatheter and at the same time not make the devices too stiff or too rigid that they are unable to still fold and pack in order to provide a superior packing or filling of the aneurysm on delivery to the aneurysm site.

[00277] In another embodiment of the invention the matrix materials for fabricating implants according to the invention are at least partially hydrophobic reticulated, elastomeric polymeric matrix. The materials are flexible and resilient in recovery, so that the implants are also compressible materials enabling the implants to be compressed and, once the compressive force is released, to then recover to, or toward, substantially their original size and shape. For example, an implant can be compressed from a relaxed configuration or a size and shape to a compressed size and shape under ambient conditions, e.g., at 25°C to fit into the introducer instrument for insertion into the vascular malformations (such as an aneurysm sac or endoleak nexus within the sac). Alternatively, an implant may be supplied to the medical practitioner performing the implantation operation, in a compressed configuration, for

example, contained in a package, preferably a sterile package. The resiliency of the elastomeric matrix that is used to fabricate the implant causes it to recover to a working size and configuration in situ, at the implantation site, after being released from its compressed state within the introducer instrument. The working size and shape or configuration can be substantially similar to original size and shape after the in situ recovery.

[00278] In another embodiment, the matrix materials for fabricating implants according to the invention are at least partially hydrophobic partially reticulated, polymeric matrix. These materials are flexible and resilient in recovery, so that the implants are partially compressible materials or non-compressible materials enabling the implants to be slightly compressed or not at all compressed during delivery through a catheter and, once they are released from the catheter to conform substantially to the internal shape and volume of the aneurysm sac. In yet another embodiment, the materials are partially reticulated or not reticulated and the polymeric matrix for fabricating implants according to the invention are still flexible and resilient in recovery, so that the implants are somewhat compressible materials or non-compressible materials enabling the implants to be slightly compressed or not at all compressed during delivery through a catheter but once they are released from the catheter to conform substantially to the internal shape and volume of the aneurysm sac. The phenomenon of conforming substantially to the internal shape and volume of the aneurysm sac will cause more effective healing of the aneurysm.

[00279] In another embodiment, the materials are at least partially hydrophobic partially reticulated, polymeric matrix for fabricating implants according to the invention are viscoelastic without being partially or substantially elastomeric. If the device or the material from which the device is made is not flexible enough or it is too stiff, the device will not be deliverable through the catheter or will not easily pushable through the tortuous contours of the catheters in the human anatomy and may even clog the catheter. The flexibility necessary for delivery through tortuous contours of

the catheters placed in the human anatomy and/or for conforming substantially to the internal shape and volume of the sac may come from the inherent flexibility or lower mechanical properties of the material and in one embodiment can be engineered from relatively stiffer materials by the creation of voids and defects in the matrix. Again, when implants according to the invention are viscoelastic without being partially or substantially elastomeric, the present invention also teaches that one or more structural filaments need not be embedded in or incorporated into the matrix.

[00280] Preferred scaffolds are reticulated elastomeric polymeric materials having sufficient structural integrity and durability to endure the intended biological environment, for the intended period of implantation. In another embodiment, scaffolds of partially reticulated, substantially reticulated or non-reticulated elastomeric polymeric materials having sufficient structural integrity and durability to endure the intended biological environment, for the intended period of implantation. In another embodiment, scaffolds of reticulated, partially reticulated, substantially reticulated or non-reticulated viscoelastic polymeric materials having sufficient structural integrity and durability to endure the intended biological environment, for the intended period of implantation. For structure and durability, at least partially hydrophobic polymeric scaffold materials are preferred although other materials may be employed if they meet the requirements described herein. Useful materials are preferably elastomeric in that they can be compressed and can resiliently recover to substantially to the pre-compression state. Alternative to reticulated polymeric materials, other materials with pores or networks of pores that may or may not be interconnected that permit biological fluids to have ready access throughout the interior of an implant may be employed, for example, woven or nonwoven fabrics or networked composites of microstructural elements of various forms.

[00281] A partially hydrophobic scaffold is preferably constructed of a material selected to be sufficiently biodurable, for the intended period of implantation that the implant will not lose its structural integrity during the implantation time in a

biological environment. The biodurable elastomeric matrices forming the scaffold do not exhibit significant symptoms of breakdown, degradation, erosion, or significant deterioration of mechanical properties relevant to their use when exposed to biological environments and/or bodily stresses for periods of time commensurate with the use of the implantable device. In one embodiment, the desired period of exposure is to be understood to be at least 29 days, preferably several weeks and most preferably 2 to 5 years or more. This measure is intended to avoid scaffold materials that may decompose or degrade into fragments, for example, fragments that could have undesirable effects such as causing an unwanted tissue response.

[00282] The void phase, preferably continuous and interconnected, of the reticulated polymeric matrix that is used to fabricate the implant of this invention may comprise as little as 50% by volume of the elastomeric matrix, referring to the volume provided by the interstitial spaces of elastomeric matrix before any optional interior pore surface coating or layering is applied. In one embodiment, the volume of void phase as just defined, is from about 20% to about 50 % of the volume of elastomeric matrix. In another embodiment, the volume of void phase as just defined, is from about 50% to about 70 % of the volume of elastomeric matrix. In another embodiment, the volume of void phase as just defined, is from about 70% to about 99% of the volume of elastomeric matrix. In another embodiment, the volume of void phase is from about 80% to about 98% of the volume of elastomeric matrix. In another embodiment, the volume of void phase is from about 90% to about 98% of the volume of elastomeric matrix. In another embodiment, the void phase is not continuous and interconnected in one or several contiguous segments of the device or is not continuous throughout the entire device.

[00283] As used herein, when a pore is spherical or substantially spherical, its largest transverse dimension is equivalent to the diameter of the pore. When a pore is non-spherical, for example, ellipsoidal or tetrahedral, its largest transverse dimension is equivalent to the greatest distance within the pore from one pore surface to another,

e.g., the major axis length for an ellipsoidal pore or the length of the longest side for a tetrahedral pore. For those skilled in the art, one can routinely estimate the pore frequency from the average cell diameter in microns.

[00284] In one embodiment relating to vascular malformation applications and the like, to encourage cellular ingrowth and proliferation and to provide adequate fluid permeability, the average diameter or other largest transverse dimension of pores is at least about 50 μm . In another embodiment, the average diameter or other largest transverse dimension of pores is at least about 100 μm . In another embodiment, the average diameter or other largest transverse dimension of pores is at least about 150 μm . In another embodiment, the average diameter or other largest transverse dimension of pores is at least about 250 μm . In another embodiment, the average diameter or other largest transverse dimension of pores is greater than about 250 μm . In another embodiment, the average diameter or other largest transverse dimension of pores is greater than 250 μm . In another embodiment, the average diameter or other largest transverse dimension of pores is at least about 275 μm . In another embodiment, the average diameter or other largest transverse dimension of pores is greater than about 275 μm . In another embodiment, the average diameter or other largest transverse dimension of pores is greater than 275 μm . In another embodiment, the average diameter or other largest transverse dimension of pores is at least about 300 μm . In another embodiment, the average diameter or other largest transverse dimension of pores is greater than about 300 μm . In another embodiment, the average diameter or other largest transverse dimension of pores is greater than 300 μm .

[00285] In another embodiment, the average diameter or other largest transverse dimension of pores is not greater than about 700 μm . In another embodiment, the average diameter or other largest transverse dimension of pores is not greater than about 600 μm . In another embodiment, the average diameter or other largest transverse dimension of pores is not greater than about 500 μm .

[00286] In one embodiment, the reticulated polymeric matrix that is used to fabricate the implants of this invention has any suitable bulk density, also known as specific gravity, consistent with its other properties. For example, in one embodiment, the bulk density may be from about 0.005 to about 0.15 g/cc (from about 0.31 to about 9.4 lb/ft³), preferably from about 0.015 to about 0.104 g/cc (from about 0.93 to about 6.5 lb/ft³) and most preferably from about 0.024 to about 0.080 g/cc (from about 1.5 to about 5.0 lb/ft³).

[00287] The polymeric matrix has sufficient tensile strength such that it can withstand normal manual or mechanical handling during its intended application and during post-processing steps that may be required or desired without tearing, breaking, crumbling, fragmenting or otherwise disintegrating, shedding pieces or particles, or otherwise losing its structural integrity. The tensile strength of the starting material(s) should not be so high as to interfere with the fabrication or other processing of elastomeric matrix. Thus, for example, in one embodiment, the reticulated polymeric matrix that is used to fabricate the implants of this invention may have a tensile strength of from about 700 to about 87,500 kg/m² (from about 1 to about 125 psi). In another embodiment, elastomeric matrix may have a tensile strength of from about 3500 to about 52,500 kg/m² (from about 5 to about 75 psi). Sufficient ultimate tensile elongation is also desirable. For example, in another embodiment, reticulated elastomeric matrix has an ultimate tensile elongation of at least about 50% to at least about 500%. In yet another embodiment, reticulated elastomeric matrix has an ultimate tensile elongation of at least 75% to at least about 300%.

[00288] One embodiment for use in the practice of the invention is reticulated or at least partially reticulated or substantially reticulated or non-reticulated elastomeric implant which is sufficiently flexible, i.e., it can be delivered from a relaxed configuration for delivery via a delivery-device, e.g., catheter, endoscope, syringe, cystoscope, trocar or other suitable introducer instrument, for delivery *in vitro* and, thereafter, into a second, working configuration *in situ*, preferably without

compressing the device during delivery through a delivery device of the invention. In another embodiment for use in the practice of the invention is a reticulated or at least partially reticulated or substantially reticulated elastomeric implant which is sufficiently resilient, i.e., resiliently-compressible, to enable it to be initially compressed under ambient conditions, e.g., at 25°C, from a relaxed configuration to a first, compact configuration for delivery via a delivery-device, e.g., catheter, endoscope, syringe, cystoscope, trocar or other suitable introducer instrument, for delivery *in vitro* and, thereafter, to expand to a second, working configuration *in situ*. In one embodiment, the device can be delivered without being compacted during delivery or it can be compacted less than 5 % of an original dimension during delivery. Furthermore, in another embodiment, an elastomeric matrix has the herein described resilient-compressibility after being compressed about 5-95% of an original dimension. In another embodiment, an elastomeric matrix has the herein described resilient-compressibility after being compressed about 10-90% of an original dimension. As used herein, elastomeric implant has "resilient-compressibility", i.e., is "resiliently-compressible", when the second, working configuration, *in vitro*, is at least about 50% of the size of the relaxed configuration in at least one dimension. In another embodiment, the resilient-compressibility of elastomeric implant is such that the second, working configuration, *in vitro*, is at least about 80% of the size of the relaxed configuration in at least one dimension. In another embodiment, the resilient-compressibility of elastomeric implant is such that the second, working configuration, *in vitro*, is at least about 90% of the size of the relaxed configuration in at least one dimension. In another embodiment, the resilient-compressibility of elastomeric implant is such that the second, working configuration, *in vitro*, is at least about 97% of the size of the relaxed configuration in at least one dimension.

[00289] In one embodiment, the device can be delivered without being compacted during delivery or it can be compacted less than 5 % of an original volume during delivery. In another embodiment, an elastomeric matrix has the herein described resilient-compressibility after being compressed about 5-95% of its original

volume. In another embodiment, an elastomeric matrix has the herein described resilient-compressibility after being compressed about 10-90% of its original volume. As used herein, "volume" is the volume swept-out by the outermost three-dimensional contour of the elastomeric matrix. In another embodiment, the resilient-compressibility of elastomeric implant is such that the second, working configuration, *in vivo*, is at least about 50% of the volume occupied by the relaxed configuration. In another embodiment, the resilient-compressibility of elastomeric implant is such that the second, working configuration, *in vivo*, is at least about 80% of the volume occupied by the relaxed configuration. In another embodiment, the resilient-compressibility of elastomeric implant is such that the second, working configuration, *in vivo*, is at least about 90% of the volume occupied by the relaxed configuration. In another embodiment, the resilient-compressibility of elastomeric implant is such that the second, working configuration, *in vivo*, occupies at least about 97% of the of volume occupied by the elastomeric matrix in its relaxed configuration.

[00290] Without being bound by any particular theory, it is believed that the absence or substantial absence of cell walls in reticulated implants when compressed to very high degree will allow them to demonstrate resilient recovery in shorter time (such as recovery time of under 15 seconds when compressed to 75% of their relaxed configuration for 10 minutes and recovery time of under 35 seconds when compressed to 90% of their relaxed configuration for 10 minutes) as compared to un-reticulated porous foams.

[00291] In one embodiment, reticulated elastomeric matrix that is used to fabricate the implants of this invention has a compressive strength of from about 700 to about 70,000 kg/m² (from about 1 to about 100 psi) at 50% compression strain. In another embodiment, reticulated elastomeric matrix has a compressive strength of from about 1,225 to about 105,000 kg/m² (from about 1.75 to about 150 psi) at 75% compression strain.

[00292] In another embodiment, reticulated elastomeric matrix that is used to fabricate the implants of this invention has a compression set, when compressed to 50% of its thickness at about 25°C, of not more than about 30%. In another embodiment, elastomeric matrix has a compression set of not more than about 20%. In another embodiment, elastomeric matrix has a compression set of not more than about 10%. In another embodiment, elastomeric matrix has a compression set of not more than about 5%.

[00293] In another embodiment, reticulated elastomeric matrix that is used to fabricate the implants of this invention has a tear strength, of from about 0.18 to about 1.78 kg/linear cm (from about 1 to about 10 lbs/linear inch).

[00294] In another embodiment of the invention the reticulated elastomeric matrix that is used to fabricate the implant can be readily permeable to liquids, permitting flow of liquids, including blood, through the composite device of the invention. The water permeability (Darcy) of the reticulated elastomeric matrix is from about 50 to about 500 (from about 0.204 to 2.04 lit/min/psi/cm/sq.cm for flow rate of water through the matrix), preferably from about 100 to about 300 (0.408 to 1.224 lit/min/psi/cm/sq.cm for flow rate of water through the matrix). In contrast, permeability (Darcy) of the unreticulated elastomeric matrix is below about 1. In another embodiment, the permeability (Darcy) of the unreticulated elastomeric matrix is below about 5.

[00295] In general, suitable biodurable reticulated elastomeric partially hydrophobic polymeric matrix that is used to fabricate the implant of this invention or for use as scaffold material for the implant in the practice of the present invention, in one embodiment sufficiently well characterized, comprise elastomers that have or can be formulated with the desirable mechanical properties described in the present specification and have a chemistry favorable to biodurability such that they provide a reasonable expectation of adequate biodurability.

[00296] Various biodurable reticulated hydrophobic polyurethane materials are suitable for this purpose. In one embodiment, structural materials for the inventive reticulated elastomers are synthetic polymers, especially, but not exclusively, elastomeric polymers that are resistant to biological degradation, for example, polycarbonate polyurethane-urea, polycarbonate polyurea-urethane, polycarbonate polyurethane, polycarbonate polysiloxane polyurethane, and polysiloxane polyurethane, and the like. Such elastomers are generally hydrophobic but, pursuant to the invention, may be treated to have surfaces that are less hydrophobic or somewhat hydrophilic. In another embodiment, such elastomers may be produced with surfaces that are less hydrophobic or somewhat hydrophilic.

[00297] The invention can employ, for implanting, a biodurable reticulatable elastomeric partially hydrophobic polymeric scaffold material or matrix for fabricating the implant or a material. More particularly, in one embodiment, the invention provides a biodurable elastomeric polyurethane scaffold material or matrix which is made by synthesizing the scaffold material or matrix preferably from a polycarbonate polyol component and an isocyanate component by polymerization, cross-linking and foaming, thereby forming pores, followed by reticulation of the porous material to provide a biodurable reticulated elastomeric product with inter-connected and/or inter-communicating pores and channels. The product is designated as a polycarbonate polyurethane, being a polymer comprising urethane groups formed from, e.g., the hydroxyl groups of the polycarbonate polyol component and the isocyanate groups of the isocyanate component. In another embodiment, the invention provides a biodurable elastomeric polyurethane scaffold material or matrix which is made by synthesizing the scaffold material or matrix preferably from a polycarbonate polyol component and an isocyanate component by polymerization, cross-linking and foaming, thereby forming pores, and using water as a blowing agent and/or foaming agent during the synthesis, followed by reticulation of the porous material to provide a biodurable reticulated elastomeric product with inter-connected and/or inter-communicating pores and channels. This product is designated as a

polycarbonate polyurethane-urea or polycarbonate polyurea-urethane, being a polymer comprising urethane groups formed from, e.g., the hydroxyl groups of the polycarbonate polyol component and the isocyanate groups of the isocyanate component and also comprising urea groups formed from reaction of water with the isocyanate groups. In all of these embodiments, the process employs controlled chemistry to provide a reticulated elastomeric matrix or product with good biodegradability characteristics. The matrix or product employing chemistry that avoids biologically undesirable or noxious constituents therein.

[00298] In one embodiment, the starting material for synthesizing the biodegradable reticulated elastomeric partially hydrophobic polymeric matrix contains at least one polyol component to provide the so-called soft segment. For the purposes of this application, the term "polyol component" includes molecules comprising, on the average, about 2 hydroxyl groups per molecule, i.e., a difunctional polyol or a diol, as well as those molecules comprising, on the average, greater than about 2 hydroxyl groups per molecule, i.e., a polyol or a multi-functional polyol. In one embodiment, this soft segment polyol is terminated with hydroxyl groups, either primary or secondary. Exemplary polyols can comprise, on the average, from about 2 to about 5 hydroxyl groups per molecule. In one embodiment, as one starting material, the process employs a difunctional polyol component in which the hydroxyl group functionality of the diol is about 2. In another embodiment, the soft segment is composed of a polyol component that is generally of a relatively low molecular weight, typically from about 500 to about 6,000 daltons and preferably between 1000 to 2500 Daltons. Examples of suitable polyol components include but not limited to polycarbonate polyol, hydrocarbon polyol, polysiloxane polyol, poly(carbonate-co-hydrocarbon) polyol, poly(carbonate-co-siloxane) polyol, poly(hydrocarbon-co-siloxane) polyol, polysiloxane polyol and copolymers and mixtures thereof.

[00299] In one embodiment, the starting material for synthesizing the biodegradable reticulated elastomeric partially hydrophobic polymeric matrix contains at least one

isocyanate component and, optionally, at least one chain extender component to provide the so-called "hard segment". In another embodiment, the starting material for synthesizing the biodurable reticulated elastomeric partially hydrophobic polymeric matrix contains at least one isocyanate component. For the purposes of this application, the term "isocyanate component" includes molecules comprising, on the average, about 2 isocyanate groups per molecule as well as those molecules comprising, on the average, greater than about 2 isocyanate groups per molecule. The isocyanate groups of the isocyanate component are reactive with reactive hydrogen groups of the other ingredients, e.g., with hydrogen bonded to oxygen in hydroxyl groups and with hydrogen bonded to nitrogen in amine groups of the polyol component, chain extender, crosslinker and/or water. In another embodiment, the average number of isocyanate groups per molecule in the isocyanate component is about 2. In another embodiment, the average number of isocyanate groups per molecule in the isocyanate component is greater than about 2 is greater than 2.

[00300] Exemplary diisocyanates include aliphatic diisocyanates, isocyanates comprising aromatic groups, the so-called "aromatic diisocyanates", and mixtures thereof. Aliphatic diisocyanates include tetramethylene diisocyanate, cyclohexane-1,2-diisocyanate, cyclohexane-1,4-diisocyanate, hexamethylene diisocyanate, isophorone diisocyanate, methylene-bis-(p-cyclohexyl isocyanate) ("H12 MDI"), and mixtures thereof. Aromatic diisocyanates include p-phenylene diisocyanate, 4,4'-diphenylmethane diisocyanate ("4,4'-MDI"), 2,4'-diphenylmethane diisocyanate ("2,4'-MDI"), polymeric MDI, and mixtures thereof. Examples of optional chain extenders include diols, diamines, alkanol amines or a mixture thereof.

[00301] In another embodiment, a small quantity of an optional ingredient, such as a multi-functional hydroxyl compound or other cross-linker having a functionality greater than 2, is present to allow cross-linking and/or to achieve a stable foam, i.e., a foam that does not collapse to become non-foamlike. Alternatively, or in addition, polyfunctional adducts of aliphatic and cycloaliphatic isocyanates can be used to

impart cross-linking in combination with aromatic diisocyanates. Alternatively, or in addition, polyfunctional adducts of aliphatic and cycloaliphatic isocyanates can be used to impart cross-linking in combination with aliphatic diisocyanates. The presence of these components and adducts with functionality higher than 2 in the hard segment component allows for cross-linking to occur.

[00302] In another embodiment, a small quantity of an optional ingredient such as 1,4 butane diol is present as a chain extender.

[00303] In one embodiment, the starting material for synthesizing the biodurable reticulated elastomeric partially hydrophobic polymeric matrix contains at least one blowing agent such as water. Other exemplary blowing agents include the physical blowing agents, e.g., volatile organic chemicals such as hydrocarbons, ethanol and acetone, and various fluorocarbons, hydrofluorocarbons, chlorofluorocarbons, and hydrochlorofluorocarbons. In another embodiment, the hard segments also contain a urea component formed during foaming reaction with water. In another embodiment, the reaction of water with an isocyanate group yields carbon dioxide, which serves as a blowing agent. The amount of blowing agent, e.g., water, is adjusted to obtain different densities of non-reticulated foams. A reduced amount of blowing agent such as water may reduce the number of urea linkages in the material.

[00304] In another embodiment, the starting material of the biodurable reticulated elastomeric partially hydrophobic polymeric matrix is a commercial polyurethane polymers are linear, not cross-linked, polymers, therefore, they are soluble, can be melted, readily analyzable and readily characterizable. In this embodiment, the starting polymer provides good biodurability characteristics. The reticulated elastomeric matrix is produced by taking a solution of the commercial polymer such as polyurethane and optionally charging it into a mold that has been fabricated with surfaces defining a microstructural configuration for the final implant or scaffold, solidifying the polymeric material and removing the sacrificial mold by melting, dissolving or subliming-away the sacrificial mold. The matrix or product

employing a foaming process that avoids biologically undesirable or noxious constituents therein. In another embodiment, the reticulated elastomeric matrix is produced by taking a solution of the commercial polymer such as polyurethane and charging it into a mold, and lyophilizing, i.e., subliming-away and removing the solvent.

[00305] Of particular interest are thermoplastic elastomers such as polyurethanes whose chemistry is associated with good biodegradability properties, for example. In one embodiment, such thermoplastic polyurethane elastomers include polycarbonate polyurethanes, polysiloxane polyurethanes, polyurethanes with so-called "mixed" soft segments, and mixtures thereof. Mixed soft segment polyurethanes are known to those skilled in the art and include, e.g., polycarbonate-polysiloxane polyurethanes. In another embodiment, the thermoplastic polyurethane elastomer comprises at least one diisocyanate in the isocyanate component, at least one chain extender and at least one diol, and may be formed from any combination of the diisocyanates, difunctional chain extenders and diols described in detail above. Some suitable thermoplastic polyurethanes for practicing the invention, in one embodiment suitably characterized as described herein, include: polyurethanes with mixed soft segments comprising polysiloxane together with a polycarbonate component.

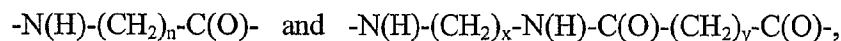
[00306] In one embodiment, the weight average molecular weight of the thermoplastic elastomer is from about 30,000 to about 500,000 Daltons. In another embodiment, the weight average molecular weight of the thermoplastic elastomer is from about 50,000 to about 250,000 Daltons.

[00307] Some commercially-available thermoplastic elastomers suitable for use in practicing the present invention include the line of polycarbonate polyurethanes supplied under the trademark BIONATE® by The Polymer Technology Group Inc. (Berkeley, CA). For example, the very well-characterized grades of polycarbonate polyurethane polymer BIONATE® 80A, 55 and 90 are soluble in THF, DMF, DMAT, DMSO, or a mixture of two or more thereof, processable, reportedly have

good mechanical properties, lack cytotoxicity, lack mutagenicity, lack carcinogenicity and are non-hemolytic. Another commercially-available elastomer suitable for use in practicing the present invention is the CHRONOFLEX® C line of biodurable medical grade polycarbonate aromatic polyurethane thermoplastic elastomers available from CardioTech International, Inc. (Woburn, MA).

[00308] In another embodiment, the starting material of the biodurable reticulated, substantially reticulated, partially reticulated or non-reticulated elastomeric partially hydrophobic polymeric matrix is a commercial viscoelastic thermoplastic including both semi-crystalline and amorphous materials, polymers, therefore, they are soluble, can be melted, readily analyzable and readily characterizable. In another embodiment, In this embodiment, the starting polymer provides good biodurability characteristics. Exemplary viscoelastic thermoplastic, although not limited only to the following list, includes suitable biocompatible polymers include polyamides, polyolefins (e.g., polypropylene, polyethylene), nonabsorbable polyesters (e.g., polyethylene terephthalate), and bioabsorbable aliphatic polyesters (e.g., homopolymers and copolymers of lactic acid, glycolic acid, lactide, glycolide, para-dioxanone, trimethylene carbonate, ϵ -caprolactone and blends thereof). Further, biocompatible polymers include film-forming bioabsorbable polymers; these include aliphatic polyesters, poly(amino acids), copoly(ether-esters), polyalkylenes oxalates, polyamides, poly(iminocarbonates), polyorthoesters, polyoxaesters including polyoxaesters containing amido groups, polyamidoesters, polyanhydrides, polyphosphazenes, biomolecules and blends thereof. For the purpose of this invention aliphatic polyesters include polymers and copolymers of lactide (which includes lactic acid d-, l- and meso lactide), ϵ -caprolactone, glycolide (including glycolic acid), hydroxybutyrate, hydroxyvalerate, para-dioxanone, trimethylene carbonate (and its alkyl derivatives), 1,4-dioxepan-2-one, 1,5-dioxepan-2-one, 6,6-dimethyl-1,4-dioxan-2-one and blends thereof.

[00309] Biocompatible polymers further include film-forming biodurable polymers with relatively low chronic tissue response, such as polyurethanes, silicones, poly(meth)acrylates, polyesters, polyalkyl oxides (e.g., polyethylene oxide), polyvinyl alcohols, polyethylene glycols and polyvinyl pyrrolidone, as well as hydrogels, such as those formed from crosslinked polyvinyl pyrrolidinone and polyesters. Other polymers, of course, can also be used as the biocompatible polymer provided that they can be dissolved, cured or polymerized. Such polymers and copolymers include polyolefins, polyisobutylene and ethylene- α -olefin copolymers; acrylic polymers (including methacrylates) and copolymers; vinyl halide polymers and copolymers, such as polyvinyl chloride; polyvinyl ethers, such as polyvinyl methyl ether; polyvinylidene halides such as polyvinylidene fluoride and polyvinylidene chloride; polyacrylonitrile; polyvinyl ketones; polyvinyl aromatics such as polystyrene; polyvinyl esters such as polyvinyl acetate; copolymers of vinyl monomers with each other and with α -olefins, such as ethylene-methyl methacrylate copolymers and ethylene-vinyl acetate copolymers; acrylonitrile-styrene copolymers; ABS resins; polyamides, such as nylon 66 and polycaprolactam; alkyd resins; polycarbonates; polyoxymethylenes; polyimides; polyethers; epoxy resins; polyurethanes; rayon; rayon-triacetate; cellophane; cellulose and its derivatives such as cellulose acetate, cellulose acetate butyrate, cellulose nitrate, cellulose propionate and cellulose ethers (e.g., carboxymethyl cellulose and hydroxyalkyl celluloses); and mixtures thereof. For the purpose of this invention, polyamides include polyamides of the general forms:



where n is an integer from about 4 to about 13; x is an integer from about 4 to about 12; and y is an integer from about 4 to about 16. It is, of course, to be understood that the listings of materials above are illustrative but not limiting.

[00310] In another embodiment the starting material of the biodurable reticulated, substantially reticulated, partially reticulated or non-reticulated partially

hydrophobic polymeric matrix are viscoelastic cross-linked and are thermosets. In some cases the viscoelastic cross-linked are elastomeric.

[00311] There are various alternative methods of making the inventive devices from the list of suitable viscoelastic biocompatible thermoplastic and cross-linked or thermoset materials and some exemplary ones include extrusion, co-extrusion, extrusion coating, solution coating, injection molding, co-injection molding, film blowing, compression molding, thermoforming, gas assisted melt extrusion with appropriate pressure release to create a porous structure, various short and long fiber composite technologies including injection molding, extrusion fiber impregnation, mesh impregnation, extrusion and injection molding of leachable fillers such as salt and sugar followed by removal of the fillers by solvent, extraction or washing, etc. While the preceding list can be considered as primary processing steps, secondary processing steps such as shaping, forming, hole punching, die punching, annealing, solid state drawing, drawing at elevated temperatures, orientation, etc. can also be used to form the inventive device from suitable viscoelastic biocompatible thermoplastic and cross-linked or thermoset materials.

[00312] Other possible embodiments of the materials used to fabricate the implants of this invention are described in co-pending, commonly assigned U.S. patent applications Serial No. 10/749,742, filed December 30, 2003, titled "Reticulated Elastomeric Matrices, Their Manufacture and Use in Implantable Devices", Serial No. 10/848,624, filed May 17, 2004, titled "Reticulated Elastomeric Matrices, Their Manufacture and Use In Implantable Devices", and Serial No. 10/990,982, filed July 27, 2004, titled "Endovascular Treatment Devices and Methods", each of which is incorporated herein by reference in its entirety.

[00313] If desired, the reticulated elastomeric implants or implants for packing the aneurysm sac or for other vascular occlusion can be rendered radiopaque to allow for visualization of the implants in situ by the clinician during and after the procedure, employing radioimaging. Any suitable radiopaque agent that can be covalently

bound, adhered or otherwise attached to the reticulated polymeric implants may be employed including without limitation, tantalum and barium sulfate. In addition to incorporating radiopaque agents such as tantalum into the implant material itself, a further embodiment of the invention encompasses the use of radiopaque metallic components to impart radiopacity to the implant. For example, thin filaments comprised of metals with shape memory properties such as platinum can be embedded into the implant and may be in the form of a straight or curved wire, helical or coil-like structure, umbrella structure, or other structure generally known to those skilled in the art. In another embodiment, thin filaments comprised of metals do not need to possess shape memory properties. Exemplary filaments include platinum or nitinol. In another embodiment, the structural fiber or components of the of structural fiber the inventive device is at least partially radiopaque. In another embodiment, radiopaque markers that are preferably metallic can be crimped at regular intervals along the device. Alternatively, a metallic frame around the implant may also be used to impart radiopacity. The metallic frame may be in the form of a tubular structure similar to a stent, a helical or coil-like structure, an umbrella structure, or other structure generally known to those skilled in the art. Attachment of radiopaque metallic components to the implant can be accomplished by means including but not limited to chemical bonding or adhesion, suturing, pressure fitting, compression fitting, and other physical methods.

[00314] Some optional embodiments of the invention comprise apparatus or devices and treatment methods employing biodegradable at least partially reticulated elastomeric implants or substantially reticulated elastomeric implants into which biologically active agents are incorporated for the matrix to be used for controlled release of pharmaceutically-active agents, such as a drug, and for other medical applications. In another embodiment, the invention comprises apparatus or devices and treatment methods employing biodegradable non-reticulated implants into which biologically active agents are incorporated for the matrix to be used for controlled release of pharmaceutically-active agents, such as a drug, and for other medical

applications. Any suitable agents may be employed as will be apparent to those skilled in the art, including, for example, but without limitation thrombogenic agents, e.g., thrombin, anti-inflammatory agents, and other therapeutic agents that may be used for the treatment of abdominal aortic aneurysms. The invention includes embodiments wherein the reticulated elastomeric material of the implants is employed as a drug delivery platform for localized administration of biologically active agents into the aneurysm sac. Such materials may optionally be secured to the interior surfaces of elastomeric matrix directly or through a coating. In one embodiment of the invention the controllable characteristics of the implants are selected to promote a constant rate of drug release during the intended period of implantation.

[00315] The implants, with reticulated structure with sufficient and required liquid permeability, permit blood or another appropriate bodily fluid to access interior surfaces of the implants, which surfaces are optionally are drug-bearing. This happens due to the presence of inter-connected, reticulated open pores that form fluid passageways or fluid permeability providing fluid access all through and to the interior of the matrix for elution of pharmaceutically-active agents, e.g., a drug, or other biologically useful materials.

[00316] In a further embodiment of the invention, the pores of biodurable reticulated elastomeric matrix that are used to fabricate the implants of this invention are coated or filled with a cellular ingrowth promoter. In another embodiment, the promoter can be foamed. In another embodiment, the promoter can be present as a film. The promoter can be a biodegradable material to promote cellular invasion of pores biodurable reticulated elastomeric matrix that are used to fabricate the implants of this invention in vivo. Promoters include naturally occurring materials that can be enzymatically degraded in the human body or are hydrolytically unstable in the human body, such as fibrin, fibrinogen, collagen, elastin, hyaluronic acid and absorbable biocompatible polysaccharides, such as chitosan, starch, fatty acids (and esters thereof), glucosylglycans and hyaluronic acid. In some embodiments, the pore

surface of the biodurable reticulated elastomeric matrix that are used to fabricate the implants of this invention is coated or impregnated, as described in the previous section but substituting the promoter for the biocompatible polymer or adding the promoter to the biocompatible polymer, to encourage cellular ingrowth and proliferation.

[00317] One possible material for use in the present invention comprises a resiliently compressible composite polyurethane material comprising a hydrophilic foam coated on and throughout the pore surfaces of a hydrophobic foam scaffold. One suitable such material is the composite foam disclosed in co-pending, commonly assigned U.S. patent applications Serial No. 10/692,055, filed October 22, 2003, Serial No. 10/749,742, filed December 30, 2003, Serial No. 10/848,624, filed May 17, 2004, and Serial No. 10/900,982, filed July 27, 2004, each of which is incorporated herein by reference in its entirety. The hydrophobic foam provides support and resilient compressibility enabling the desired collapsing of the implant for delivery and reconstitution *in situ*.

[00318] The reticulated biodurable elastomeric and at least partially hydrophilic material can be used to carry a variety of therapeutically useful agents, for example, agents that can aid in the healing of the aneurysm, such as elastin, collagen or other growth factors that will foster fibroblast proliferation and ingrowth into the aneurysm, agents to render the foam implant non-thrombogenic, or inflammatory chemicals to foster scarring of the aneurysm. Furthermore the hydrophilic foam, or other agent immobilizing means, can be used to carry genetic therapies, e.g. for replacement of missing enzymes, to treat atherosclerotic plaques at a local level, and to release agents such as antioxidants to help combat known risk factors of aneurysm.

[00319] Pursuant to the present invention it is contemplated that the pore surfaces may employ other means besides a hydrophilic foam to secure desired treatment agents to the hydrophobic foam scaffold.

[00320] The agents contained within the implant can provide an inflammatory response within the aneurysm, causing the walls of the aneurysm to scar and thicken. This can be accomplished using any suitable inflammation inducing chemicals, such as sclerosants like sodium tetradecyl sulphate (STS), polyiodinated iodine, hypertonic saline or other hypertonic salt solution. Additionally, the implant can contain factors that will induce fibroblast proliferation, such as growth factors, tumor necrosis factor and cytokines.

[00321] The fibers used in the present invention for as a component of reinforcing filaments is polymeric and may be made using a variety of processes that provide fibers with the desired properties (such as modulus, tensile strength, elongation etc.). Those skilled in the art of fiber processing are well versed in the art of extrusion, solution spinning etc. which may be used to provide polymer based fibers. These fibers may be oriented or drawn using conventional process to provide the desired degree of modulus, strength, elongation, etc. Generally, a fiber orientation process is used to improve the properties of the reinforcing fibers. Suitable organic biocompatible polymer that can be used to make the polymeric fibers are well known in the art and include both bioabsorbable and biostable polymers.

[00322] For example, bioabsorbable polymeric fiber can be made from a polymer or copolymer or blend containing glycolide, L-lactide, D-lactide, caprolactone, para-dioxanone and/or trimethylene carbonate and combinations thereof.

[00323] Suitable organic biocompatible biostable polymeric fiber can be made from include but are not limited to polymers selected from the group consisting of polyesters (such as polyethylene terephthalate and polybutylene terephthalate), polyolefins (such as polyethylene and polypropylene including atactic, isotactic, syndiotactic, and blends thereof as well as, polyisobutylene and ethylene-alphaolefin copolymers), polyamides (such as nylon 4, nylon 6, nylon 66, nylon 610, nylon 11, nylon 12), acrylic polymers and copolymers, polycarbonates, polyurethanes and their

copolymers, blends and combinations thereof.

[00324] In another embodiment, the fibers used in the present invention for as a component of reinforcing filaments can be made from glass fibers or carbon fiber, the likes of which are commonly used to reinforce polymeric composites.

[00325] The fibers used in the present invention for as a component of reinforcing filaments can have a diameter that range from 0.01 mm to 0.40 mm and preferably from 0.02 mm to 0.30 mm. In one embodiment, the fibers used in the present invention for as a component of reinforcing filaments can be any commercially available, non-absorbable polymeric or absorbable suture.

EXAMPLES

Example 1: Fabrication of a Cross-linked Reticulated Polyurethane Matrix

The aromatic isocyanate RUBINATE 9258 (from Huntsman) was used as the isocyanate component. RUBINATE 9258, which is a liquid at 25°C, contains 4,4'-MDI and 2,4'-MDI and has an isocyanate functionality of about 2.33. A diol, poly(1,6-hexanecarbonate)diol (POLY-CD CD220 from Arch Chemicals) with a molecular weight of about 2,000 Daltons was used as the polyol component and was a solid at 25°C. Distilled water was used as the blowing agent. The blowing catalyst used was the tertiary amine triethylenediamine (33% in dipropylene glycol; DABCO 33LV from Air Products). A silicone-based surfactant was used (TEGOSTAB® BF 2370 from Goldschmidt). A cell-opener was used (ORTEGOL® 501 from Goldschmidt). The viscosity modifier propylene carbonate (from Sigma-Aldrich) was present to reduce the viscosity. The proportions of the components that were used are set forth in the following table:

Table 2.

<u>Ingredient</u>	<u>Parts by Weight</u>
Polyol Component	100
Viscosity Modifier	5.80
Surfactant	0.66
Cell Opener	1.00
Isocyanate Component	47.25
Isocyanate Index	1.00
Distilled Water	2.38
Blowing Catalyst	0.53

The polyol component was liquefied at 70°C in a circulating-air oven, and 100 g thereof was weighed out into a polyethylene cup. 5.8 g of viscosity modifier was added to the polyol component to reduce the viscosity, and the ingredients were mixed at 3100 rpm for 15 seconds with the mixing shaft of a drill mixer to form "Mix-1". 0.66 g of surfactant was added to Mix-1, and the ingredients were mixed as described above for 15 seconds to form "Mix-2". Thereafter, 1.00 g of cell opener was added to Mix-2, and the ingredients were mixed as described above for 15 seconds to form "Mix-3". 47.25 g of isocyanate component were added to Mix-3, and the ingredients were mixed for 60 ± 10 seconds to form "System A".

2.38 g of distilled water was mixed with 0.53 g of blowing catalyst in a small plastic cup for 60 seconds with a glass rod to form "System B".

System B was poured into System A as quickly as possible while avoiding spillage. The ingredients were mixed vigorously with the drill mixer as described above for 10 seconds and then poured into a 22.9 cm x 20.3 cm x 12.7 cm (9 in. x 8 in. x 5 in.) cardboard box with its inside surfaces covered by aluminum foil. The foaming profile was as follows: 10 seconds mixing time, 17 seconds cream time, and 85 seconds rise time.

Two minutes after the beginning of foaming, i.e., the time when Systems A and B were combined, the foam was placed into a circulating-air oven maintained at 100-105°C for curing for from about 55 to about 60 minutes. Then, the foam was removed from the oven and cooled for 15 minutes at about 25°C. The skin was removed from each side using a band saw. Thereafter, hand pressure was applied to each side of the foam to open the cell windows. The foam was replaced into the circulating-air oven and postcured at 100-105°C for an additional four hours.

The average pore diameter of the foam, as determined from optical microscopy observations, was greater than about 275 μm .

The following foam testing was carried out according to ASTM D3574: Bulk density was measured using specimens of dimensions 50 mm x 50 mm x 25 mm. The density was calculated by dividing the weight of the sample by the volume of the specimen. A density value of 2.81 lbs/ft³ (0.0450 g/cc) was obtained.

Tensile tests were conducted on samples that were cut either parallel to or perpendicular to the direction of foam rise. The dog-bone shaped tensile specimens were cut from blocks of foam. Each test specimen measured about 12.5 mm thick, about 25.4 mm wide, and about 140 mm long; the gage length of each specimen was 35 mm, and the gage width of each specimen was 6.5 mm. Tensile properties (tensile strength and elongation at break) were measured using an INSTRON Universal Testing Instrument Model 1122 with a cross-head speed of 500 mm/min (19.6 inches/minute). The average tensile strength perpendicular to the direction of foam rise was determined as 29.3 psi (20,630 kg/m²). The elongation to break perpendicular to the direction of foam rise was determined to be 266%.

The measurement of the liquid flow through the material is measured in the following way using a liquid permeability apparatus or Liquid Permeater (Porous Materials, Inc., Ithaca, NY). The foam sample was 8.5 mm in thickness and covered a hole 6.6 mm in diameter in the center of a metal plate that was placed at the bottom of the Liquid Permeater device filled with water. Thereafter, the air pressure above the sample was increased slowly to extrude the liquid from the sample, and the permeability of water (Darcy) through the foam was determined to be 0.11.

Example 2: Reticulation of a Cross-linked Polyurethane Foam

Reticulation of the foam described in Example 1 was carried out by the following procedure: A block of foam measuring approximately 15.25 cm x 15.25 cm x 7.6 cm (6 in. x 6 in. x 3 in.) was placed into a pressure chamber, the doors of the chamber were closed, and an airtight seal to the surrounding atmosphere was maintained. The pressure within the chamber was reduced to below about 100 millitorr by evacuation for at least about two minutes to remove substantially all of the air in the foam. A mixture of hydrogen and oxygen gas, present at a ratio sufficient to support combustion, was charged into the chamber over a period of at least about three minutes. The gas in the chamber was then ignited by a spark plug. The ignition exploded the gas mixture within the foam. The explosion was believed to have at least partially removed many of the cell walls between adjoining pores, thereby forming a reticulated elastomeric matrix structure.

The average pore diameter of the reticulated elastomeric matrix, as determined from optical microscopy observations, was greater than about 275 μm . A scanning electron micrograph image of the reticulated elastomeric matrix of this example (not shown here) demonstrated, e.g., the communication and interconnectivity of pores therein.

The density of the reticulated foam was determined as described above in Example 1. A post-reticulation density value of 2.83 lbs/ft^3 (0.0453 g/cc) was obtained.

Tensile tests were conducted on reticulated foam samples as described above in Example 1. The average post-reticulation tensile strength perpendicular to the direction of foam rise was determined as about 26.4 psi (18,560 kg/m^2). The post-reticulation elongation to break perpendicular to the direction of foam rise was determined to be about 250%. The average post-reticulation tensile strength parallel to the direction of foam rise was determined as about 43.3 psi (30,470 kg/m^2). The

post-reticulation elongation to break parallel to the direction of foam rise was determined to be about 270%.

Compressive tests were conducted using specimens measuring 50 mm x 50 mm x 25 mm. The tests were conducted using an INSTRON Universal Testing Instrument Model 1122 with a cross-head speed of 10 mm/min (0.4 inches /minute). The post-reticulation compressive strengths at 50% compression, parallel to and perpendicular to the direction of foam rise, were determined to be 1.53 psi (1,080 kg/m²) and 0.95 psi (669 kg/m²), respectively. The post-reticulation compressive strengths at 75% compression, parallel to and perpendicular to the direction of foam rise, were determined to be 3.53 psi (2,485 kg/m²) and 2.02 psi (1,420 kg/m²), respectively. The post-reticulation compression set, determined after subjecting the reticulated sample to 50% compression for 22 hours at 25°C then releasing the compressive stress, parallel to the direction of foam rise, was determined to be about 4.5%.

The resilient recovery of the reticulated foam was measured by subjecting 1 inch (25.4 mm) diameter and 0.75 inch (19 mm) long foam cylinders to 75% uniaxial compression in their longitudinal direction for 10 or 30 minutes and measuring the time required for recovery to 90% ("t-90%") and 95% ("t-95%") of their initial length. The percentage recovery of the initial length after 10 minutes ("r-10") was also determined. Separate samples were cut and tested with their length direction parallel to and perpendicular to the foam rise direction. The results obtained from an average of two tests are shown in the following table:

Table 3.

Time compressed (min)	Test Sample Orientation	t-90% (sec)	t-95% (sec)	r-10 (%)
10	Parallel	6	11	100
10	Perpendicular	6	23	100
30	Parallel	9	36	99
30	Perpendicular	11	52	99

In contrast, a comparable foam with little to no reticulation typically has t-90 values of greater than about 60-90 seconds after 10 minutes of compression.

The measurement of the liquid flow through the material is measured in the following way using a liquid permeability apparatus or Liquid Permeater (Porous Materials, Inc., Ithaca, NY). The foam samples were between 7.0 and 7.7 mm in thickness and covered a hole 8.2 mm in diameter in the center of a metal plate that was placed at the bottom of the Liquid Permeater device filled with water. The water was allowed to extrude through the sample under gravity, and the permeability of water (Darcy) through the foam was determined to be 180 in the direction of foam rise and 160 in the perpendicular to foam rise.

Example 3: Fabrication of a Cross-linked Reticulated Polyurethane Matrix

A cross-linked Polyurethane Matrix was made using similar starting materials and following procedures similar to the one described in Example 1. The starting ingredients were same except for the following. The aromatic isocyanate Mondur MRS-20 (from Bayer AG) was used as the isocyanate component. Mondur MRS-20 (from Bayer AG), which is a liquid at 25°C, contains 4,4'-MDI and 2,4'-MDI and has an isocyanate functionality of about 2.3. Glycerol or Glycerin 99.7% USP/EP (from Dow Chemicals) was used as a cross-linker and 1,4-Butanediol (from BASF Chemical) was used as chain extender. The cross-linker and the chain extender are mixed into system B. The proportions of the components that were used are set forth in the following table:

Table 4.

<u>Ingredient</u>	<u>Parts by Weight</u>
PolyCD™CD220(g)	100
Propylene carbonate (g)	5.80
Tegostab BF-2370 (g)	1.50
Ortegol 501 (g)	2.00
Mondur MRS-20 (g)	51.32
Isocyanate index	1.0
Distilled water) (g)	1.89
Glycerine (g)	2.15
Chain extender (g)	0.72
Dabco 33 LV (g)	0.56

The reaction profile is as follows:

Mixing time of System A and System B before pouring into cardboard box (seconds)	10
Cream time (seconds)	27
Rise time (seconds)	120

Reticulation of the foam described above was carried out by the following procedure: A block of foam measuring approximately 15.25 cm x 15.25 cm x 7.6 cm (6 in. x 6 in. x 3 in.) was placed into a pressure chamber, the doors of the chamber were closed, and an airtight seal to the surrounding atmosphere was maintained. The pressure within the chamber was reduced to below about 100 millitorr by evacuation for at least about two minutes to remove substantially all of the air in the foam. A mixture of hydrogen and oxygen gas, present at a ratio sufficient to support combustion, was charged into the chamber over a period of at least about three minutes. The gas in the chamber was then ignited by a spark plug. The ignition exploded the gas mixture within the foam. The explosion was believed to have at least partially removed many of the cell walls between adjoining pores, thereby forming a reticulated elastomeric matrix structure.

A second reticulation was performed on the once reticulated elastomeric matrix structure using similar condition reticulation parameters as described above to yield a reticulated elastomeric matrix structure in which cell walls between adjoining pores were further removed.

A scanning electron micrograph image of the reticulated elastomeric matrix of this example (not shown here) demonstrated, e.g., the communication and interconnectivity of pores therein.

The average pore diameter of the twice reticulated elastomeric matrix, as determined from optical microscopy observations, was greater than about 222 μm .

The following foam testing was carried out according to ASTM D3574: Bulk density was measured using specimens of dimensions 50 mm x 50 mm x 25 mm. The density was calculated by dividing the weight of the sample by the volume of the specimen. A density value of 4.3 lbs/ft³ (0.069 g/cc) was obtained.

Tensile tests of twice reticulated elastomeric matrix were conducted on samples that were cut perpendicular to the direction of foam rise. The dog-bone shaped tensile specimens were cut from blocks of foam. Each test specimen measured about 12.5 mm thick, about 25.4 mm wide, and about 140 mm long; the gage length of each specimen was 35 mm, and the gage width of each specimen was 6.5 mm. Tensile properties (tensile strength and elongation at break) were measured using an INSTRON Universal Testing Instrument Model 1122 with a cross-head speed of 500 mm/min (19.6 inches/minute). The average tensile strength perpendicular to the direction of foam rise was determined as 37.2 psi (26,500 kg/m²). The elongation to break perpendicular to the direction of foam rise was determined to be 89 %. The average tensile strength parallel to the direction of foam rise was determined as 70.4 psi (49,280 kg/m²). The elongation to break perpendicular to the direction of foam rise was determined to be 109 %.

Compressive tests of twice reticulated elastomeric matrix were conducted using specimens measuring 50 mm x 50 mm x 25 mm. The tests were conducted using an INSTRON Universal Testing Instrument Model 1122 with a cross-head speed of 10 mm/min (0.4 inches /minute). The post-reticulation compressive strengths parallel to the direction of foam rise at 50% and 75 % compression strains were determined to be 3.3 psi (2,310 kg/m²) and 10.7 psi (7,490 kg/m²), respectively.

The compression set of twice reticulated elastomeric matrix, determined after subjecting the reticulated sample to 50% compression for 22 hours at 25°C then releasing the compressive stress, parallel to the direction of foam rise, was determined to be about 5.1 %.

The permeability of water (Darcy) through the twice reticulated elastomeric matrix was determined to be 226 in the direction of foam rise.

Example 4: Implant Assembly, Processing, and Testing

An experiment was performed to assess the pushability of different NEUROSTRINGTM implant configurations based on various combinations of structural filaments. The material in Example 2 is used as the starting matrix for an implant according to the invention. Different combinations of structural filaments were used in the study, either multifilament fiber corresponding to fiber equivalent 7-0 polyester suture and/or platinum wire measuring 0.0015" – 0.0030" in diameter.

To create each implant prototype, a 2 mm sheet of the elastomeric matrix material was loaded into a commercial sewing machine. In the top bobbin, 7-0 multifilament fiber corresponding to 7-0 polyester suture available in a spool format (Genzyme) was used. In the bottom bobbin, a single platinum wire or a rope composite (7-0 multi-filament fiber corresponding to 7-0 polyester suture + platinum wire or platinum wire + platinum wire) was used as outlined in Table 5 below. The rope composites were created by using a coil winder to create a twisted composite of two filaments. After being sewn with the filaments, the elastomeric matrix was cut to the required implant length. The elastomeric matrix with the structural filaments was then trimmed under a microscope using surgical scissors (Fine Science Tools) to an outer diameter of 0.022" – 0.023". Platinum markers were then positioned over the length of the implant at 1.0 cm increments and crimped in place manually using tweezers.

The implants were attached to a pusher/detachment system. Each implant was pushed through a clear, custom-made 0.027" ID microcatheter for a total of five passes to verify the pushability of the string. Pushability was selected as the most clinically relevant outcome measure which serves as a proxy for the stiffness or mechanical strength of the string. If the string was not pushable at the original length, the string was trimmed shorter to evaluate pushable length. The outcome of the pushability testing is set forth in the following table:

TABLE 5.

Implant Prototype Number	Wire / Rope Configuration for Bottom Bobbin	Fiber Type for Top Bobbin	String Length (cm)	String Dia. (inch)	MC ID (inch)	Pushable Y/N	Comments
1	7-0 suture / .003" PT rope	7-0 suture	24	.023	.027	Y	String starts to buckle after 3 passes through the microcatheter
2	.003" Platinum Wire	7-0 suture equivalent	22	.018	.027	Y	No buckling at all
3	.003" Platinum Wire	7-0 suture equivalent	18.5	.026	.027	Y	Some buckling @ 4 th pass
4a	.002" Platinum Wire	7-0 suture equivalent	24	.022	.027	N	
4b	.002" Platinum Wire	7-0 suture equivalent	20	.022	.027	N	
4c	.002" Platinum Wire	7-0 suture equivalent	15	.022	.027	N	
4d	.002" Platinum Wire	7-0 suture equivalent	10	.022	.027	Y	Some buckling @ 2 nd pass
5	7-0 Suture	7-0 suture equivalent	N/A	N/A	N/A	N	Ultra Soft string-not pushable
6a	Secant Suture / .0015" (2) PT Wire	7-0 suture equivalent	17	.032	.033	N	
6b	Secant Suture / .0015" (2) PT Wire	7-0 suture equivalent	10	.032	.033	Y	Buckling @ 1 st pass
7a	7-0 Suture / .002" (2) PT Rope	7-0 suture equivalent	22	.023	.027	N	
7b	7-0 Suture / .002" (2) PT Rope	7-0 suture equivalent	15	.023	.027	Y	Buckling @ 1 st pass
7c	7-0 Suture / .002" (2) PT Rope	7-0 suture equivalent	10	.023	.027	Y	Trimmed shorter - buckling @ 2 nd pass
8	7-0 suture / .003" (2)PT rope	7-0 suture equivalent	18.5	.024	.027	Y	No buckling at all
9a	7-0 suture / .00225" (2)PT rope	7-0 suture equivalent	25	.024	.027	N	
9b	7-0 suture / .00225" (2)PT rope	7-0 suture equivalent	15	.024	.027	Y	Trimmed shorter – no buckling

Different types of implants according to the invention employing different combinations of structural filaments can be manufactured, and they have different functionalities.

Example 5 - Mechanical performance of Implant

For select prototypes, an INSTRON Universal Testing Instrument was used to determine the tensile properties of the implant prototypes. The implants were made by a process similar to the one described in Example 4 but using matrix material made in accordance to Example 3 . For these tested prototypes, three samples of 3.8 cm length each were tested at a crosshead speed of 2.54 cm/min and with the gauge length set at 0.7 inch (1.8 cm). The results were as follows:

Table 6.

String Configuration (Wire / Suture)	Length of implant	Avg. Dia. (inch)	Tensile load to failure (Newtons)	Stiffness or slope of load vs extension curve (Newtons/mm).
0.002" PT + fiber equivalent to 7-0 Polyester	8	0.02	5.7	19.2
0.002" (X 2) + fiber equivalent to 7-0 Polyester	8	0.02	7.2	46.8

Clearly, the mechanical properties of the implant according to the invention can be varied or engineered by the type and number of the reinforcing filament or fiber.

Example 6: Histological Evaluation of a Plurality of Cross-linked Reticulated Polyurethane Matrix Implants in a Canine Carotid Bifurcation Aneurysm Model

An established animal model of cerebral aneurysms was used to evaluate the histologic outcomes of implanting a plurality of cylindrical implants machined from a block of cross-linked reticulated polyurethane matrix as described in Example 2. The three animals were sacrificed at the three-month timepoint to assess tissue response to the cross-linked reticulated polyurethane matrix.

One of two different implant configurations was used in this experiment. The first configuration was a cylindrical implant measuring 6 mm diameter x 15 mm length. The second configuration was a segmented, cylindrical implant measuring 3 mm diameter x 15 mm length. To machine the implants, a rotating die cutter was used to cut 3 mm and 6 mm diameter cylinders. The implants were then trimmed to 15 mm in length. Implant dimensions were tested for acceptability by use of calipers and visualization under a stereo-microscope, with acceptance of implants measuring +/- 5% of target dimensions.

An aneurysm was surgically created at the carotid arterial bifurcation of three dogs. This model simulates the hemodynamics of a human saccular aneurysm, which typically occurs at an arterial bifurcation. After one month, a second embolization procedure was performed in which a plurality of implants machined from a block of cross-linked reticulated polyurethane matrix was delivered into the aneurysm sac using a guide catheter. The 6x15 mm cylindrical implants were delivered using a commercially available 7 Fr Cordis Vista-Brite guide catheter. The 3x15 mm cylindrical implants were delivered using a commercially available 5 Fr Cordis Vista-Brite guide catheter. A loader apparatus was used to pull compress the implants from their expanded state into a compressed state for introduction through the hemostasis valve of the guide catheter. An obturator was then used to push the compressed implant from the proximal end of the guide catheter to the distal end, where the

implant was deployed in a slow, controlled manner into the aneurysm sac.

A plurality of implants was used in each of the three dogs to achieve post-procedural angiographic occlusion as shown in Table 7 below. Platinum coil markers (0.003" diameter) embedded in the central lumen of the implants allowed the implants to be readily visualized under standard fluoroscopy, to verify implant deployment, placement, and positioning.

Table 7.

Dog #	Aneurysm Dimensions (mm)	Aneurysm Volume (mm³)	6x15 mm Implants (n)	3x15 mm Implants (n)
BMX-1	22.4mm L x 10.1mm W	1884 mm ³	2	5
BMX-2	18.9mm L x 8.8mm W	1207 mm ³	4	9
BMX-3	23 mm L x 11 mm W	2295 mm ³	12	0

At three months following the embolization procedure, the animals were sacrificed to assess tissue response to the cross-linked reticulated polyurethane matrix. For histology processing, samples were dehydrated in a graded series of ethanol and embedded in methylmethacrylate plastic. After polymerization, each aneurysm was bisected (sawn) longitudinally by the Exakt method and glued onto a holding block for sectioning using a rotary microtome at 5 – 6 microns. The sections were mounted on charged slides and stained with hematoxylin-eosin and Movat pentachrome stains. All sections were examined by light microscopy for the presence inflammation, healing response, calcification and integrity of the wall at the neck interface and surrounding aneurysm.

Gross observation indicated that the aneurysm sac was fully packed with no open spaces. There was nearly complete pannus growth on the luminal surface at the proximal neck interface with focal, luminal invagination (pocket).

Longitudinal section through the proximal neck of the aneurysm showed greater than 95% luminal occlusion of aneurysm sac by reticulated polyurethane matrix. The luminal surface at the proximal interface showed almost complete covering by fibrous tissue with overlying endothelialization as shown in Figure 25, which is 20X magnification showing fibrocollagenous tissue surrounding implant material and extending to luminal surface at proximal neck interface. There was nearly complete healing of tissue ingrowth surrounding the implanted material characterized by the presence of fibrocollagenous tissue (light-green and yellow by Movat Pentachrome stain) as shown in Figure 26, which is a low power (4X) Movat stain of the apex of the aneurysm showing marked fibrocollagenous tissue ingrowth. There was minimal, focal organizing granulation tissue surrounding material (predominantly at the center of the occluded aneurysm) with mild, chronic inflammation consisting of lymphocytes and some giant cells, consistent with the healing response. There was almost complete replacement of elastic lamellae by fibrocollagenous tissue. No calcification was observed.

The histological response to the reticulated polyurethane matrix in this experiment demonstrated that the material can serve as a scaffold to support extensive organic tissue ingrowth with minimal inflammation and thereby holds promise as a bioactive solution to the treatment of cerebral aneurysms.

Example 7: Angiographic Outcomes from Use of Reticulated Polyurethane Implants in a Canine Carotid Bifurcation Aneurysm Model

An established animal model of cerebral aneurysms was used to evaluate the angiographic outcomes of implanting a 0.030" implants according to the invention made from cross-linked reticulated polyurethane matrix as described in Example 2.

To create the implants, thin sheets measuring 2.0 mm in depth were sliced from a block of reticulated polyurethane matrix. A sewing machine was then used to stitch surgical suture measuring 0.003" in diameter through the thin foam sheet to form a straight line. Individual strings were cut by using micro-scissors to trim around the suture line under a microscope until the final outer diameter of 0.030" (outside edge of the foam string) was achieved. Implant dimensions were tested for acceptability by delivering each individual string through a custom-made 3.5Fr (0.035" inner diameter) microcatheter. Platinum bands were hand-crimped every 1.0 cm along the length of each implant to impart radiopacity.

An aneurysm was surgically created at the carotid arterial bifurcation of three dogs. This model simulates the hemodynamics of a human saccular aneurysm, which typically occurs at an arterial bifurcation. After one month, a second embolization procedure was performed as follows. After preparing the access site using standard surgical technique, a 6Fr Boston Scientific Guide Catheter with Straight Tip was advanced to the aneurysm. A Boston Scientific Excelsior 3Fr Microcatheter was then advanced through the guide catheter into the aneurysm neck. One or two GDC-18 framing coils were then deployed through the microcatheter to frame the aneurysm. After positioning and detaching the framing coil, the Excelsior microcatheter was withdrawn. A custom-made 3.5Fr (0.035" inner diameter) microcatheter was then advanced through the guide catheter into the aneurysm neck. The implant, loader, and pusher wire were removed from their sterile packaging. The loaded implant and microcatheter were flushed with sterile saline. The loader/implant was then introduced into the hemostasis valve of the microcatheter. The implant was

subsequently delivered into the aneurysm by pushing the implant with the pusher wire while using hydraulic assistance through the 3.5Fr custom microcatheter. The implant was positioned and detached into the aneurysm. The pusher wire was removed from the microcatheter and an angiogram was performed to confirm occlusion. Implants ranging from 10 – 18 cm in length were deployed as necessary until angiographic occlusion was confirmed.

Table 8 below shows the quantities and volumes of framing coils and implants used in each of the three animals. All 22 implants were successfully delivered using hydraulic assistance and controlled mechanical detachment. Post-procedure angiographic occlusion was achieved in all three animals, with minor neck remnants.

Table 8.

Dog #	Aneurysm Dimensions	Framing Coil Qty	Total Implant Length (cm)	Number of Implant Implants
BMX-4	13.2mm L x 12.1mm W	2	59.0 cm	5
BMX-5	14.0mm L x 10.2mm W	1	100.5 cm	8
BMX-6	15.6mm L x 10.2mm W	1	109.5 cm	9

At two-week follow-up, an angiogram was performed to assess angiographic outcomes including device stability (compaction) and aneurysm recanalization. All three dogs showed stable or progressing occlusion with no device compaction and no evidence of aneurysm recanalization. The angiographic series from BMX-5 is shown in Figures 27A to 27C, where Figure 27A represents pre-embolization, Figure 27B represents post embolization, and Figure 27C represents follow-up.

The angiographic outcomes at two-week follow-up demonstrated that implants according to the invention can be utilized for the embolization of cerebral aneurysms. This experiment showed the implant of the invention is consistently deliverable through a 3Fr microcatheter, and that the implants are stable with no evidence of device compaction, no migration, and no aneurysm recanalization at the two-week followup timepoint.

Example 8: Effects of Packing Density on Angiographic Outcomes Using Reticulated Polyurethane Implants in a Canine Carotid Bifurcation Aneurysm Model

An established animal model of cerebral aneurysms was used to evaluate the impact of different packing densities on angiographic outcomes for two different configurations of implants machined from a block of cross-linked reticulated polyurethane matrix as described in Example 2. The study evaluated the efficacy of different packing densities using (i) cylindrical implants (3mm x 15mm, 6mm x 15mm) machined as described in Example 5; and (ii) 0.030" implants machined as described in Example 7. Packing density effectiveness was measured as angiographic occlusion and device stability (no compaction) at two-week follow-up.

Table 9 below shows that packing densities ranging from 40% – 350% result in angiographic occlusion at two-week follow-up with stable or progressing occlusion and no device compaction. The one exception, BMX-1, was noted to occur in a dog with an unusual, giant, unstable aneurysm that continued to expand even at the two-week angiographic follow-up timepoint.

Table 9.

Dog #	Aneurysm Volume (mm³)	Packing Density (%)	Embolization Agents (Reticulated Matrix "RM" and/or GDC-18 Coils)	2W Angiographic Outcomes vs. Baseline
PILOT	1457.0 mm ³	349.2%	• 12-6x15mm RM Cylinders	• 100% occlusion • No recanalization
BMX-1	1907.8 mm ³	166.7%	• 6-6x15mm RM Cylinders • 6-3x15mm RM Cylinders	• Recanalization
BMX-2	1196.3 mm ³	115.2%	• 2-6x15mm RM Cylinders • 5-3x15mm RM Cylinders	• Progressing thrombosis • No device compaction
BMX-3	766.3 mm ³	345.8%	• 4-6x15mm RM Cylinders • 5-3x15mm RM Cylinders	• Stable occlusion • No device compaction
BMX-4	1011.8 mm ³	39.6%	• 2-GDC-18 coils • 59.0 cm RM Implant	• No recanalization • No device compaction
BMX-5	762.6 mm ³	78.7%	• 1-GDC-18 coil • 100.5 cm RM Implant	• Progressive occlusion • No device compaction
BMX-6	849.7 mm ³	76.6%	• 1-GDC-18 coil • 109.5 cm RM Implant	• Progressive occlusion • No device compaction

This experiment demonstrated that various configurations of implants machined from reticulated polyurethane matrix can be utilized to embolize large aneurysms in a wide range of packing densities (40% – 350%) with efficacious angiographic outcomes at two-week follow-up.

Example 9: Histological Evaluation of 0.030" Diameter Implants
in a Canine Carotid Bifurcation Aneurysm Model

An established animal model of cerebral aneurysms was used to evaluate the angiographic outcomes of implanting 0.030" NEUROSTRING™ implants according to the invention made from cross-linked reticulated polyurethane matrix as described in Example 2.

The implants were prepared as described in Example 7. Thin sheets measuring 2.0 mm in depth were sliced from a block of reticulated polyurethane matrix. A sewing machine was then used to stitch 7-0 surgical polyester suture with 0.003" diameter through the thin foam sheet to form a straight line. Individual strings were cut by using micro-scissors to trim around the suture line under a microscope until the final outer diameter of 0.030" (outside edge of the foam string) was achieved. Implant dimensions were tested for acceptability by delivering each individual string through a custom-made 3.5Fr (0.035" inner diameter) microcatheter. Platinum bands (90% Pt, 10% Ir, 0.016 in. i.d., 0.002 in. wall, 0.030 in. length) were hand-crimped every 1.0 cm along the length of each implant to impart radiopacity.

The animal model and surgical procedure were also performed as described in Example 7. An aneurysm was surgically created at the carotid arterial bifurcation of three dogs. This model simulates the hemodynamics of a human saccular aneurysm, which typically occurs at an arterial bifurcation. After one month, a second embolization procedure was performed as follows: After preparation of the access site using standard surgical technique, a 6Fr Boston Scientific Guide Catheter with Straight Tip was advanced to the aneurysm. A Boston Scientific Excelsior 3Fr Microcatheter was then advanced through the guide catheter into the aneurysm neck. A single GDC-18 framing coil measuring either 14mm x 30 cm (BMX-5) or 16mm x 30 cm (BMX-6) was then deployed through the microcatheter to frame the aneurysm. After positioning and detaching of the framing coil, the Excelsior microcatheter was withdrawn. A custom-made 3.5Fr (0.035" inner diameter) microcatheter was then

advanced through the guide catheter into the aneurysm neck. The implant, loader, and pusher wire were removed from their sterile packaging. The loaded implant and microcatheter were flushed with sterile saline. The loader/implant was then introduced into the hemostasis valve of the microcatheter. The implant was subsequently delivered into the aneurysm by pushing the implant with the pusher wire while using hydraulic assistance through the 3.5Fr custom microcatheter. The implant was positioned and detached into the aneurysm. The pusher wire was removed from the microcatheter and an angiogram was performed to confirm occlusion. Implants ranging from about 10 to 18 cm in length were deployed as necessary until angiographic occlusion was confirmed:

The table below outlines the aneurysm dimensions, test article utilization and packing density in this study:

Table 10.

Dog #	Aneurysm Dimensions	Aneurysm Volume (mm ³)	Total Length of Implant (cm)	Embolization Agent Volume (mm ³)	Number of Implants	Packing Density (%)
BMX-5	14.0mm L x 10.2mm W x 6.4mm Neck	762.6 mm ³	100.5 cm	600.0 mm ³	8	78.7%
BMX-6	15.6mm L x 10.2mm W x 6.7mm Neck	849.7 mm ³	109.5 cm	650.7 mm ³	9	76.6%

Both animals were sacrificed at the three-month timepoint for histological evaluation. For histology processing, samples were dehydrated in a graded series of ethanol and embedded in methylmethacrylate plastic. After polymerization, each aneurysm was bisected (sawn) longitudinally by the Exakt Method. The Exakt sections were glued onto plastic slides for grinding and polishing to 25 - 30 microns thickness and stained with Toluidine Blue. All sections were examined by light microscopy for the presence inflammation, healing response, calcification and integrity of the wall at the neck interface and surrounding aneurysm.

Grossly, there was nearly complete pannus growth on the luminal surface at the proximal neck interface indicating good sealing of the neck interface. A longitudinal section through the proximal neck of the aneurysm showed total occlusion of the aneurysm sac by the Neurostring implant and surrounding coil framing. The luminal surface at the neck interface showed complete covering by neointima formation with overlying endothelialization. The periphery of the sac showed thin to thick tissue healing (in-growth) with minimal to mild chronic inflammation (normal healing response) surrounding the implants. The inner two thirds of the aneurysm sac was densely packed with the embolic material and surrounded by minimal to mild organizing granulation tissue with fibrin deposition. There was minimal to mild chronic inflammation consisting of predominantly of macrophages and some giant cells.

The effectiveness of the implant according to the invention can be appreciated in Figures 28A to 28C. Figure 28A is a low power (1.25 magnification)(TB stained) micrograph of a longitudinal (Exakt) section through the proximal neck of the aneurysm showing complete neointimal coverage of neck surface and total occlusion of aneurysm sac by embolic material in subject BMX-5. Figure 28B is a high power micrograph of a representative section showing the center (core) of the aneurysm for the same subject with progressive healing characterized by granulation tissue (pink staining) with fibrin surrounding the embolic material (void spaces). Figure 28C is a

high power micrograph showing thin to thick tissue ingrowth (T) at the periphery of the aneurysm for the subject BMX-6 and surrounding underlying embolic implant material (*).

Thus, there was effective occlusion in the canine carotid bifurcation aneurysm model of aneurysms treated with NEUROSTRINGTM implants by the three-month timepoint. Each of the treated aneurysms showed complete healing (neointima formation) and confluent endothelialization of the neck surface with adequate incorporation of organizing granulation tissue surrounding the embolic material at the periphery of the sac. In both samples, the center of the sac showed adequate distribution of embolic material characterized by minimal to partial organization and fibrin deposition, indicative of the healing process underway. Overall, both samples show minimal to mild chronic inflammation, which is associated with the normal tissue healing response.

Example 10: Manufacture of 0.016" NEUROSTRINGTM Implant with Continuous Reinforcing Filament Structure

The aromatic isocyanate MONDUR MRS 20 (from Bader) was used as the isocyanate component. MRS 20, which is a liquid at 25°C, contains 4,4'-MDI and 2,4'-MDI and has an isocyanate functionality of about 2.3. Glycerine (99.9% Purity) from DOW and 1,4 Butane Diol (BDO from BASF) were used as cross-linker and chain extender, respectively. A diol, poly(1,6-hexanecarbonate)diol (POLY-CD CD220 from Arch Chemicals) with a molecular weight of about 2,000 Daltons was used as the polyol component and was a solid at 25°C. Distilled water was used as the blowing agent. The catalyst used was the tertiary amine triethylenediamine (33% in dipropylene glycol; DABCO 33LV from Air Products). Two silicone-based surfactants, (TEGOSTAB® BF 2370 and TEGOSTAB BF 8305 from Goldschmidt) were used. A cell-opener was used (ORTEGOL® 501 from Goldschmidt). The viscosity modifier propylene carbonate (from Sigma-Aldrich) was present to reduce the viscosity. The proportions of the components that were used to make the matrix

are set forth in the following table:

Table 11.

<u>Ingredient</u>	<u>Parts by Weight</u>
Polyol Component	100
Viscosity Modifier	5.80
Surfactant 1 (BF2370)	0.70
Surfactant 1 (BF8305)	0.55
Cell Opener	2.00
Isocyanate Component	53.26
Isocyanate Index	1.00
Distilled Water	2.38
Glycerin	2.15
1,4 BDO	0.72
Blowing Catalyst	0.45

The polyol component was liquefied at 68°C, the isocyanate component was at 24 °C, and the water premixed with and containing all the other additives was also at 24 °C in separate mixing tanks of a 3-component Edgesweet Bench Top Machine for making polyurethane. All three components were mixed by a single-shot method in a high shear pin-style mixing chamber at approximately 5000 rpm. The foaming profile was as follows: 10 seconds cream time, and 120 to 140 seconds rise time.

The foam was placed into a circulating-air oven maintained at 90°C for curing for from about 55 to about 60 minutes. Then, the foam was removed from the oven and cooled for 15 minutes at about 25°C. The skin was removed from each side using a band saw. Thereafter, hand pressure was applied to each side of the foam to open the cell windows. The foam was replaced into the circulating-air oven and post-cured at 90C for an additional four hours.

Reticulation of the foam was carried out by following the procedure in Example 2.

The density of the reticulated foam was determined as described above in Example 1. A post-reticulation density value of 3.23 lbs/ft³ (0.052 g/cc) was obtained. Tensile tests were conducted on reticulated foam samples as described above in Example 1. The average post-reticulation tensile strength perpendicular to the direction of foam rise was determined as about 39.9 psi (28,050 kg/m²). The post-reticulation elongation to break perpendicular to the direction of foam rise was determined to be about 135 %. The average post-reticulation tensile strength parallel to the direction of foam rise was determined as about 55 psi (38,670 kg/m²). The post-reticulation elongation to break parallel to the direction of foam rise was determined to be about 126%. Compressive tests were conducted reticulated foam samples as described above in Example 2. The post-reticulation compressive strengths at 50% compression, parallel to the direction of foam rise, were determined to be 2.3 psi (1,620kg/m²). The post-reticulation compression set, determined after subjecting the reticulated sample to 50% compression for 22 hours at 25°C then releasing the compressive stress, parallel to the direction of foam rise, was determined to be about 7.5%.

The material, made above, used as the starting matrix for an implant according to the invention, and was cut into a 2 mm sheet of the elastomeric matrix material using a rotary splitter for polyurethane foam (Fecken-Kirfel Peeler).

To create an implant prototype with a continuous reinforcing filament structure, a continuous subassembly was first created as follows: First, platinum wire ranging in diameter from 0.001" - 0.005" was helically wound onto a polymeric core fiber, comprised of polyester or polypropylene. The winding was performed using a coil winder to create a final subassembly comprised of a continuous platinum coil with a filamentous core with o.d. of 0.003" to 0.010" and length from 0.5 cm – 50 cm.

The continuous platinum coil subassembly was then inserted into a 2 mm sheet of the elastomeric matrix using a needle to longitudinally draw the subassembly into the sheet. After being pull inserted into elastomeric matrix, the matrix was cut to the

required implant length. The elastomeric matrix with the continuous reinforcing filament was then trimmed under a microscope using surgical scissors (Fine Science Tools) to an outer diameter of 0.030" to 0.040", forming an initial elongated structure. An external filament, 9-0 polyester, was then loosely wrapped on a diagonal bias (helical pattern) with spacing of 1mm between each consecutive wrap to secure the elastomeric matrix to the subassembly and this is called the string.

A combination of mechanical deformation with the application of thermal energy was then utilized to adhere the elastomeric matrix to the subassembly in the string and also to downsize the diameter from the initial elongated structure to the final target diameter to make the 0.016" NEUROSTRING™ implant. In this process, the string is loaded into pre-expanded LDPE (low density polyethylene) tubing of i.d.=0.065 inches and exposed to a heat source (Hotbox) @ 360 °F to compress the elastomeric matrix component in the string such that the final LDPE tubing i.d.=0.019 inches. After the compression process, the LDPE tubing is peeled away from the compressed implant. In the final assembly step, proximal and distal coils are secured to the ends of the implant, which is then attached to a pusher/detachment system.

While illustrative embodiments of the invention have been described, it is, of course, understood that various modifications of the invention will be obvious to those of ordinary skill in the art. Such modifications are within the spirit and scope of the invention which is limited and defined only by the appended claims.

WE CLAIM:

1. A occlusion device comprising a flexible, longitudinally extending elastomeric matrix member, wherein the device assumes a non-linear shape capable of conformally filling a targeted vascular site.
2. The device of Claim 1 which also comprises at least one longitudinally extending reinforcing filament or fiber.
3. The device of Claim 2, wherein each filament or fiber is selected from the group consisting of platinum wire, platinum coil, platinum hypo-tube, platinum band, polymeric fiber or filament, a braid of platinum wire and polymeric fiber or filament, and a braid of two or more platinum wires
4. The device of Claim 2, wherein each reinforcing filament or fiber is inserted into the elastomeric matrix member.
5. The device of Claim 4, wherein the elastomeric matrix member is adhered to each reinforcing filament or fiber.
6. The device of Claim 2, wherein there are at least two reinforcing filaments or fibers.
7. The device of Claim 6, wherein there are two reinforcing filaments or fibers.
8. The device of Claim 6, wherein the reinforcing filaments or fibers are selected from materials preselected to vary at least one physical property of the device.
9. The device of Claim 8, wherein the physical property is stiffness.
10. The device of Claim 8, wherein the physical property comprises modulus of elasticity.

11. The device of Claim 6, wherein the reinforcing filaments or fibers are knotted or looped together at various points to secure the elastomeric matrix member.

12. The device of Claim 11, where the reinforcing filaments or fibers are knotted together by radiopaque bands.

13. The device of Claim 2, wherein at least one reinforcing filament or fiber is radiopaque.

14. The device of Claim 1, wherein the elastomeric matrix is a biodurable, reticulated elastomeric matrix.

15. The device of Claim 1, wherein the elastomeric matrix is a polycarbonate polyurethane-urea, polycarbonate polyurea-urethane, polycarbonate polyurethane, or polycarbonate polysiloxane polyurethane.

16. The device of Claim 1, wherein the elastomeric matrix is resiliently recoverable.

17. A method of occluding an aneurysm or vessel which comprises deploying or inserting a device of Claim 1 into an aneurysm or vessel.

18. A packaging or introducer system comprising:
an introducer sheath having a longitudinally extending lumen and proximal and distal ends;
an occlusion device of Claim 1 positioned within said lumen, said occlusion device having a proximal end;
a side arm attached to the proximal end of the introducer sheath and having a hemostasis valve and a flusher port; and
a pusher member extending through the hemostasis valve into the introducer sheath and having a distal end removably engaged to the proximal end of the occlusion device.

19. The system of Claim 18, wherein an interlocking wire having a distal end extends longitudinally into the pusher member, the occlusion device has a loop at its proximal end, the distal end of the pusher member has an opening through which said loop extends, the distal end of the interlocking wire is releasably held within the distal end of the pusher member, and the distal end of the interlocking wire releasably engages said loop so that the distal end of the pusher member releasably engages the proximal end of the occlusion device.

20. The system of Claim 19, wherein the distal end of the interlocking wire and the distal end of the pusher member are both radiopaque.

21. A method for occluding a vessel or aneurysm comprising:
introducing an introducer system of Claim 18 into a delivery catheter having a longitudinally extending lumen and proximal and distal ends with hydraulic assistance;

withdrawing the introducer sheath and side arm, leaving the occlusion device positioned within the lumen of the delivery catheter;

advancing the occlusion device using the pusher member and hydraulic assistance to position the occlusion device within a targeted vascular site;

disengaging the pusher member from the occlusion device; and
withdrawing the pusher member.

22. A vascular occlusion device comprising:
a flexible, longitudinally extending biocompatible member, and
at least one longitudinally extending component engaged with the biocompatible member to secure the biocompatible member and assist it in conformally filling a targeted vascular site.

23. The device of Claim 22 which assumes a non-linear shape to conformally fill a targeted vascular site.

24. The device of Claim 22 which comprises a non-curvilinear shape in at least one portion of the member.

25. The device of Claim 24, wherein the non-curvilinear shape comprises at least one vertex.

26. The device of Claim 25, wherein the at least one vertex comprises a plurality of vertices.

27. The device of Claim 26, wherein the plurality of vertices permit chain-like folding of the device.

28. The device of Claim 22, wherein the biocompatible member comprises an elastomeric matrix.

29. The device of Claim 28, wherein the elastomeric matrix is a biodurable, reticulated elastomeric matrix.

30. The device of Claim 28, wherein the elastomeric matrix is selected from the group consisting of polycarbonate polyurethane-urea, polycarbonate polyurea-urethane, polycarbonate polyurethane, and polycarbonate polysiloxane polyurethane.

31. The device of Claim 28, wherein the elastomeric matrix comprises resiliently recoverable material.

32. The device of Claim 22, wherein each longitudinally extending component comprises a structural filament.

33. The device of Claim 22, wherein the at least one longitudinally extending components comprise a polymeric fiber or filament and at least one wire element.

34. The device of Claim 33, wherein the at least one wire element comprises a continuous wire.

35. The device of Claim 33, wherein the at least one wire element comprises a plurality of staples.

36. The device of Claim 35, wherein the plurality of staples are interlocked pairwise to form a chain.

37. The device of Claim 22 which comprises at least two longitudinally extending components that are coupled to each other at a plurality of locations.

38. The device of Claim 37, wherein the components are coupled by knotting.

39. The device of Claim 22, wherein the at least one longitudinally extending components comprise at least two structural filaments or fibers.

40. The device of Claim 39, wherein there are two structural filaments or fibers.

41. The device of Claim 39, wherein the structural filaments or fibers are selected from materials preselected to vary at least one physical property of the device.

42. The device of Claim 41, wherein the physical property is stiffness.

43. The device of Claim 41, wherein the physical property comprises modulus of elasticity.

44. The device of Claim 39, wherein each structural filament or fiber is selected from the group consisting of platinum wire, platinum coil, platinum hypotube, platinum band, polymeric fiber or filament, a braid of platinum wire and polymeric fiber or filament, and a braid of two or more platinum wires.

45. The device of Claim 39, where the structural filaments are knotted together by radiopaque bands.

46. The device of Claim 22, wherein at least one longitudinally extending component comprises radiopaque material.

47. The device of Claim 37, wherein the material of each component and the coupling between the at least two components are selected to produce a desired physical property of the device.

48. The device of Claim 47, wherein the desired physical property of the device comprises a stiffness in at least one portion of the device.

49. The device of Claim 48, wherein the stiffness in at least one portion of the device comprises a stiffness at a location of coupling and the stiffness comprises a stiffness relative to a stiffness of the device at a point substantially distant from the point of coupling.

50. An introducer system for a vascular occlusion device, the vascular occlusion device having a proximal end and a distal end, the distal end having a contact element, the system comprising:

an introducer component having a longitudinally extending lumen and proximal and distal ends;

a pusher component slidable within the introducer component, the pusher component having a distal end positioned adjacent to the distal end of the occlusion device; and

a core component having a distal end and extending through the pusher component and parallel to the occlusion device so that the distal end of the core component contacts the contact element, thereby applying a tensile force to the occlusion device.

51. The system of Claim 50, further comprising:

an interlocking wire having a distal end extending longitudinally into the pusher member,

wherein:

the occlusion device has a release element at its proximal end,
the distal end of the pusher component has an opening through which
the release element extends,
the distal end of the interlocking wire is releasably held within the distal
end of the pusher member, and
the distal end of the interlocking wire releasably engages the release
element so that the distal end of the pusher component releasably engages the
proximal end of the occlusion device.

52. The system of Claim 50, wherein the release element comprises a loop.

53. The system of Claim 50, wherein the contact element comprises a
tensioning element.

54. A method for occluding a targeted vascular site comprising:

introducing an introducer system into a delivery catheter having a
longitudinally extending lumen and proximal and distal ends, the introducer system
carrying a vascular occlusion device and having a pusher component;

withdrawing the introducer system, leaving the vascular occlusion
device positioned within the lumen of the delivery catheter;

advancing the vascular occlusion device using the pusher component to
position the vascular occlusion device within the targeted vascular site;

disengaging the pusher component from the occlusion device; and
withdrawing the pusher.

55. A device for occluding a targeted vascular site comprising:

an elongate occluding element comprising a material permitting
ingrowth of tissue at the targeted vascular site; and

a plurality of features provided along the occluding element, the features
selected to confer material characteristics allowing the creation of vertices in the
element.

56. The device according to Claim 55, wherein the plurality of features are provided along the occluding element at preselected locations.

57. The device according to Claim 55, wherein the vertices facilitate packing of the occluding element into the targeted vascular site.

58. The device according to Claim 55, wherein at least one of the features comprises a topological characteristic of the elongate element.

59. The device according to Claim 55, further comprising a second element engaged with the elongate element, wherein at least one of the features comprises a topological characteristic of the second element.

60. The device according to Claim 59, further comprising a third element engaged with the elongate element, wherein at least one of the features comprises a relationship between the second and third elements.

61. The device according to Claim 59, wherein the elongate element comprises a biodegradable material permitting vascular tissue ingrowth and the second element comprises a polymeric fiber or filament.

62. The device according to Claim 61, wherein the topological characteristic of the polymeric fiber or filament comprises a stitch.

63. The device according to Claim 60, wherein the relationship between the second and third elements comprises a knot.

64. The device according to Claim 55, wherein at least one of the group consisting of a dimension of a feature and a distance between a pair of features is preselected to facilitate packing of the targeted vascular site.

65. A method for treating a condition at a targeted vascular site comprising:
providing an elongate occlusion device comprising biocompatible
material;

introducing the occlusion device into the targeted vascular site; and
while introducing the occlusion device, inducing at least one
noncurvilinear geometry in the occlusion device.

66. The method of Claim 65, wherein inducing at least one non-curvilinear
geometry produces a geometry of the occlusion device that packs the targeted vascular
site in a substantially conformal manner.

67. The method of Claim 65, wherein the at least one non-curvilinear
geometry comprises a plurality of folds.

68. The method of Claim 67, wherein inducing a plurality of folds produces
a chain-like occlusion device for packing the targeted vascular site in a substantially
conformal manner.

69. The method of Claim 65, wherein the occlusion device comprises a
biocompatible material.

70. The method of Claim 69, wherein the biocompatible material comprises
a material permitting ingrowth of tissue at the targeted site.

71. The method of Claim 70, wherein the occlusion device is introduced to
permanently biointegrate at the targeted site.

72. A method for treating an aneurysm in a mammal, comprising:
providing an elongate biocompatible, biodurable material permitting
tissue ingrowth at the site of the aneurysm; and

introducing the biocompatible, biodurable material at the site of the aneurysm in a quantity sufficient to occlude the aneurysm and to permit permanent biointegration of the occlusion device in the aneurysm.

73. The method of Claim 72, wherein the biocompatible, biodurable material is a reticulated elastomeric matrix.

74. A method for treating an aneurysm comprising introducing sufficient biocompatible material into the aneurysm to pack the aneurysm with the material to a packing density of from at least about 10% to at least about 200%.

75. The method of Claim 74, wherein the biocompatible material comprises a flexible, longitudinally extending biocompatible member.

76. The method of Claim 74, wherein the aneurysm is a cerebral aneurysm.

77. The method of Claim 74, wherein the biocompatible material comprises non-swellable material.

78. A mechanism for detaching a vascular implant from a delivery device, the vascular implant having a proximal end and a coupling component at its proximal end, the mechanism comprising:

an engagement element coupled at a distal end of the delivery device, the engagement element having a first, engaged position and a second, disengaged position; and

an energy transfer component coupled to the engagement element at a distal portion of the component to actuate the engagement element;

wherein the engagement element, when actuated, engages the coupling component of the implant when in the first position and releases the coupling component when in the second position.

79. The mechanism of Claim 78, wherein the coupling component of the implant comprises a flexible structure.

80. The mechanism of Claim 79, wherein the flexible structure comprises at least one opening through which an aspect of the engagement element of the delivery device may pass when in the first, engaged position.

81. The mechanism of Claim 80, wherein the flexible structure comprises a loop.

82. The mechanism of Claim 78, wherein the engagement element comprises a structure that moves, along an axis, from the first position to the second position.

83. The mechanism of Claim 82, wherein the delivery device comprises at least one of the group consisting of a wire and a sheath, the axis is parallel to the longitudinal axis of the delivery device, and the energy transfer component comprises at least one of the wire and the sheath.

84. The mechanism of Claim 83, wherein the delivery device comprises a sheath and the energy transfer component comprises a wire, and wherein the engagement element transitions between the first position and the second position as a result of a relative rotation of the wire engagement element with respect to the delivery device sheath.

85. The mechanism of Claim 84, wherein the engagement element comprises a distal portion of the wire, the coupling component of the implant comprises a loop structure, and wherein, in the first position of the engagement element, the loop structure is stably retained about a distal portion of the wire and, wherein, in the second position of the engagement element, the loop structure is released over a free distal end of the wire.

86. The mechanism of Claim 85, wherein:
the distal portion of the wire has threads that engage mating threads coupled to the sheath,
the delivery device comprises a distal portion having a side wall with an aperture through which the loop structure passes and is held in place when the engagement element is in the first position, and
when the engagement element is in the second position, the distal end of the wire is proximal of the aperture, releasing the loop structure and allowing it to exit through the aperture.

87. The mechanism of Claim 78, wherein the control element is operable by a practitioner.

88. A method for fabricating a vascular occlusion device, comprising:
providing a biocompatible material adapted for tissue ingrowth and capable of being formed into at least one elongate element having a longitudinal axis and dimensioned for vascular insertion;
engaging at least one support element with the biocompatible material to at least partially lie substantially along at least a portion of the longitudinal axis of the at least one elongate element; and
forming the elongate element from the biocompatible material substantially in the vicinity of the longitudinal axis.

89. The method of Claim 88, wherein the elongate element comprises a flexible linear element.

90. The method of Claim 89, wherein the at least one support element comprises a structural filament engaged with the biocompatible material substantially along at least a portion of its longitudinal axis.

91. The method of Claim 90, wherein the at least one support element comprises a polymeric fiber or filament.

92. The method of Claim 91, wherein the polymeric fiber or filament is stitched to the biocompatible material.
93. The method of Claim 91, wherein the polymeric fiber or filament is engaged with the biocompatible material with at least one adhesive.
94. The method of Claim 92, wherein the stitching is performed by a sewing machine.
95. The method of Claim 91, wherein the at least one support element further comprises a second support element.
96. The method of Claim 95, wherein the second support element comprises a staple.
97. The method of Claim 95, wherein the at least one support element comprises at least two staples interlocking with one another form a chain.
98. The method of Claim 95, wherein the at least one second support element comprises a radiopaque material.
99. The method of Claim 95, wherein the at least one second support element comprises wire.
100. The method of Claim 99, wherein the wire is coupled to the suture at a plurality of points.
101. The method of Claim 100, wherein the coupling at at least one of the plurality of points comprises a knot.
102. The method of Claim 95, wherein the at least one support element comprises at least two elements including a braided platinum wire/polymeric fiber or filament subassembly and a polymeric fiber or filament element.

103. The method of Claim 95, wherein the at least second support element comprises a plurality of staples.

104. The method of Claim 103, wherein the staples are spaced apart from one another.

105. The method of Claim 88, wherein forming the elongate element from the biocompatible material and the engaged support element comprises separating the elongate element and the support element from adjoining material.

106. The method of Claim 105, wherein separating is accomplished by cutting.

107. The method of Claim 106, further comprising removing excess material so that the elongate element has a preselected maximum width.

108. The method of Claim 88, further comprising coupling or engaging a visualizable element proximate to the end of the elongate element.

109. The method of Claim 108, wherein the visualizable end unit comprises a coil.

110. The method of Claim 108, wherein the end unit comprises radiopaque material.

111. The method of Claim 88, wherein engaging at least one support element with the biocompatible material precedes forming the elongate element from the biocompatible material, whereby the elongate element so formed includes the at least one support element.

112. The method of Claim 88, wherein forming the elongate element from the biocompatible material precedes engaging at least one support element with the biocompatible material.

113. A method of treating an aneurysm comprising:
providing a biocompatible element having a form that comprises no predefined geometry; and
introducing the biocompatible element to conformally fill the aneurysm.

114. The method of Claim 113, wherein introducing the biocompatible material comprises application of the material to a wall of the aneurysm in such a manner that material curves upon itself to produce segments of the material.

115. The method of Claim 114, wherein the material segments so applied are arranged in a brush stroke form.

116. The method of Claim 114, wherein the segments, although substantially parallel to the wall of the aneurysm, each have a spatial orientation, and the spatial orientations of the segments are substantially randomly distributed with respect to one another.

117. The method of Claim 114, wherein the segments are defined *in situ* by vertices in the material.

118. The method of Claim 114, wherein the segments are defined by curved portions of the material that lack vertices.

119. The method of Claim 113, wherein introducing the material to conformally fill the aneurysm comprises application of a first layer of the material directly adjacent a wall of the aneurysm and a second layer substantially overlaying the first layer.

120. The method of Claim 119, further comprising applying additional layers until the aneurysm is substantially occluded.

121. The method of Claim 113, wherein introducing the biocompatible element to fill the aneurysm comprises the deposition of the material in the manner of a viscous liquid flow.

122. The method of Claim 113, wherein the material has a stiffness preselected to produce, when the material is fully introduced into the aneurysm, a packing density of from at least about 10% to at least about 200%.

123. The method of Claim 113, wherein introducing the biocompatible material to fill the aneurysm comprises the deposition of the material in the manner of a piece of cooked spaghetti to form a string ball in the aneurysm.

124. A vascular occlusion device comprising a string-shaped biocompatible element having a plurality of concavities for accommodating ingrowth of vascular tissue.

125. The vascular occlusion device of Claim 124, wherein the concavities comprise pores.

126. The vascular occlusion device of Claim 124, wherein the concavities together form a honeycomb structure.

127. The vascular occlusion device of Claim 124, wherein the concavities together form a reticulated porous structure.

128. The vascular occlusion device of Claim 124, wherein the concavities comprise a plurality of fragmentary pores.

129. The vascular occlusion device of Claim 124, substantially excluding complete pores.

130. The vascular occlusion device of Claim 124, wherein the concavities comprise cavities.

131. The vascular occlusion device of Claim 124, wherein the concavities comprise concave surfaces formed in the exterior surface of the member.

132. The vascular occlusion device of Claim 124, wherein, when the member is packed into an aneurysm, concavities are positioned adjacent one another and at least some of the adjacent concavities in neighboring portions of the member together form virtual pores to accommodate tissue ingrowth.

133. A vascular occlusion device comprising:
a flexible, longitudinally extending biocompatible member for delivery through a lumen of a delivery device;
the member comprising a plurality of pores having a dimensional characteristic selected on the basis of a minimum interior dimension of the lumen.

134. The vascular occlusion device of Claim 133, wherein the interior dimension of the lumen comprises the inner diameter of the lumen, and the member has a maximum width less than the minimum interior dimension of the lumen.

135. The vascular occlusion device of Claim 134, wherein the pore size is selected in order that the average pore diameter is greater than or equal to about 25% of the maximum width of the member.

136. The vascular occlusion device of Claim 135, wherein the pore size is selected in order that the average pore diameter is from about 25% to about 33% of the maximum diameter of the member.

137. A system for adjusting the properties of a longitudinally extending device, comprising:
(a) a flexible, longitudinally extending member and
(b) at least one longitudinally extending component engaged with member (a) ,
wherein component (b) is selected from materials preselected to vary at least one physical property of the device.

138. The system of Claim 137, wherein member (a) is biocompatible.
139. The system of Claim 137, wherein component (b) is selected from the group consisting of platinum, iridium, and polymeric fibers or filaments.
140. The system of Claim 137, wherein there are at least two longitudinally extending components.

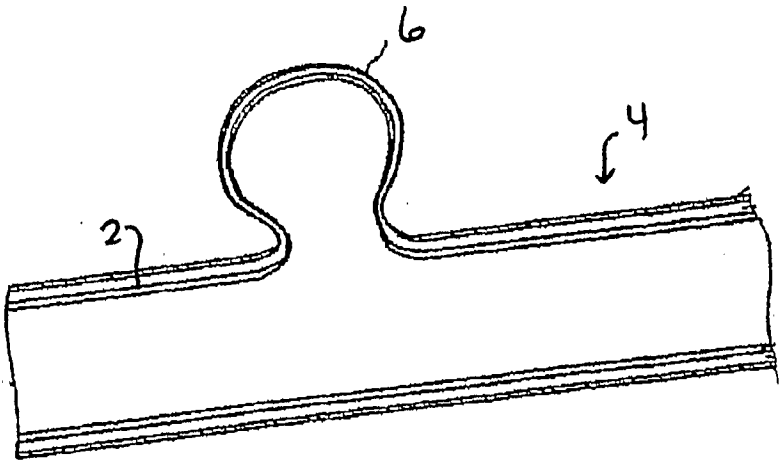


Figure 1

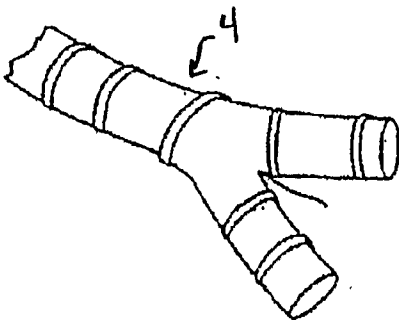


Figure 2

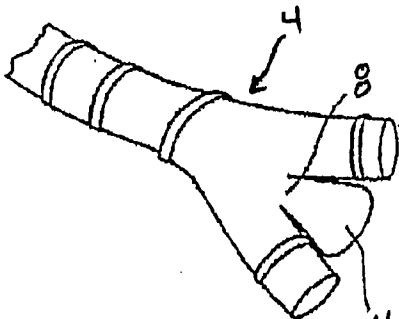


Figure 3

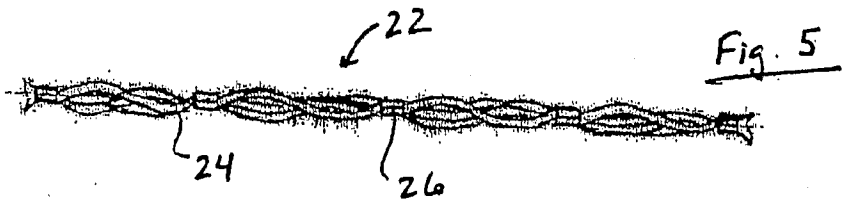
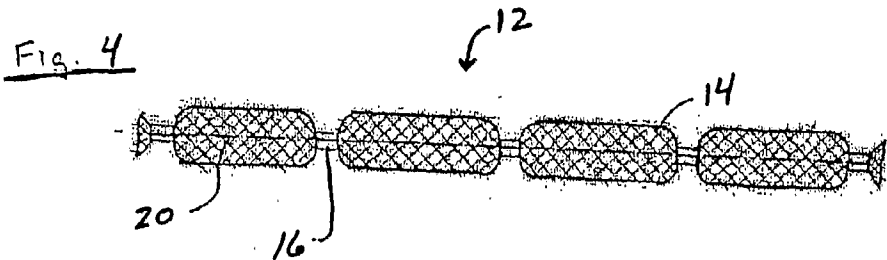


Fig. 6

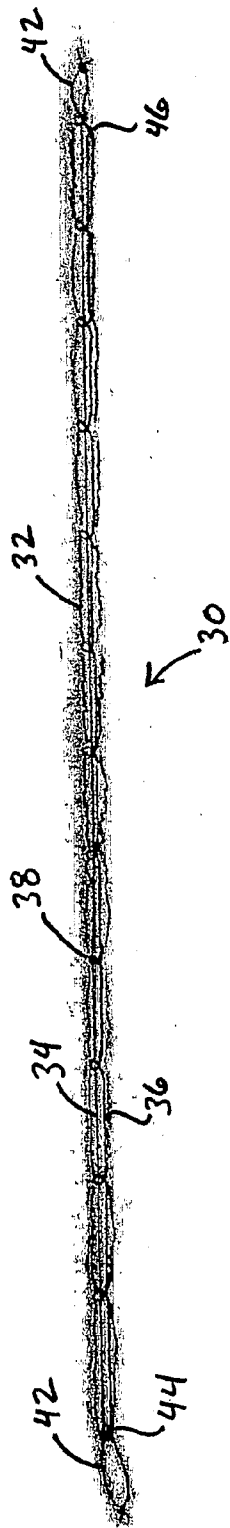
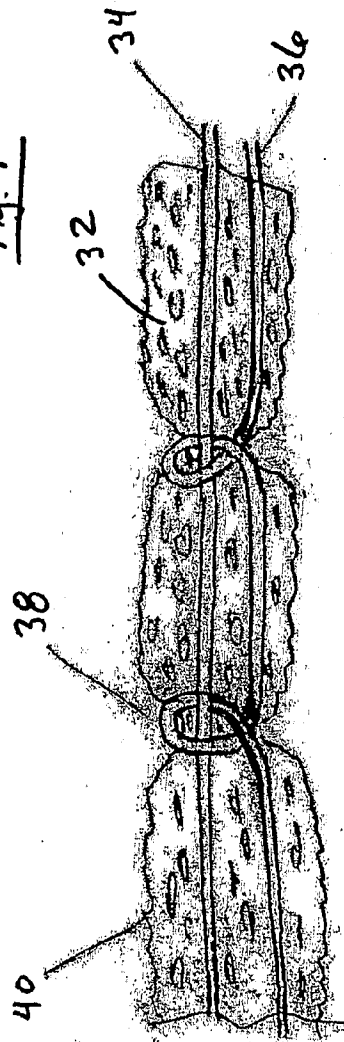


Fig. 7



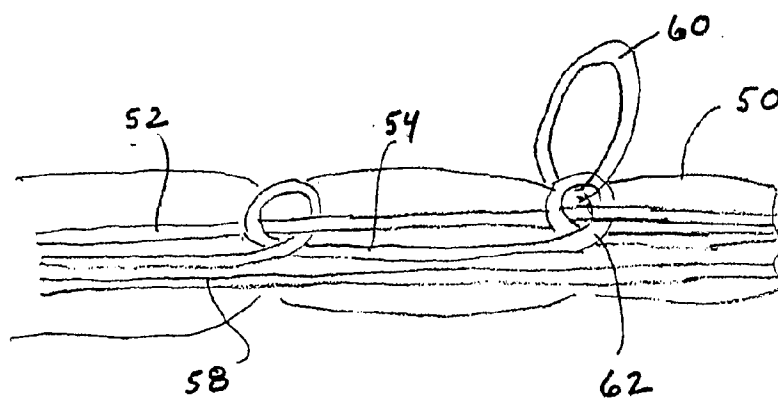


Fig. 8

Fig. 9

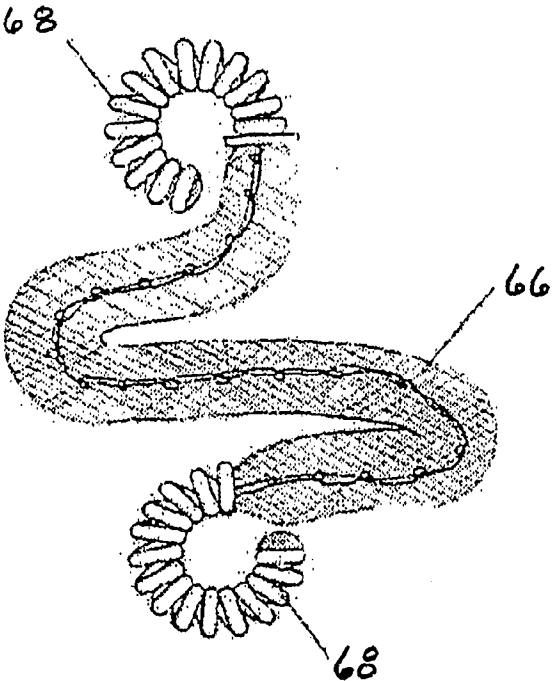


FIG. 10A

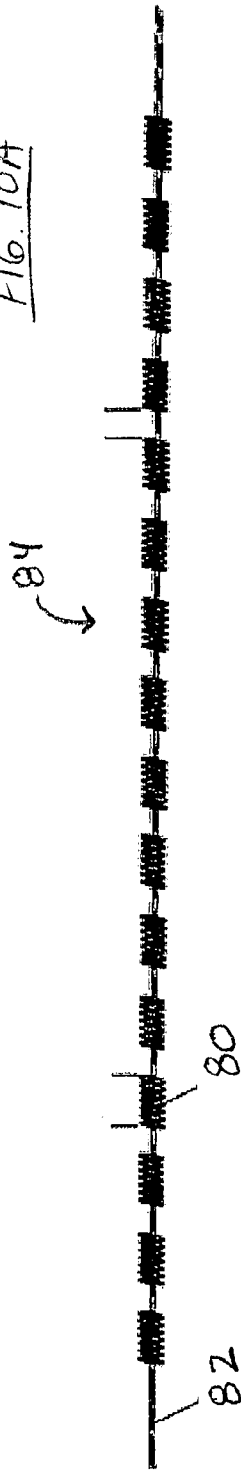
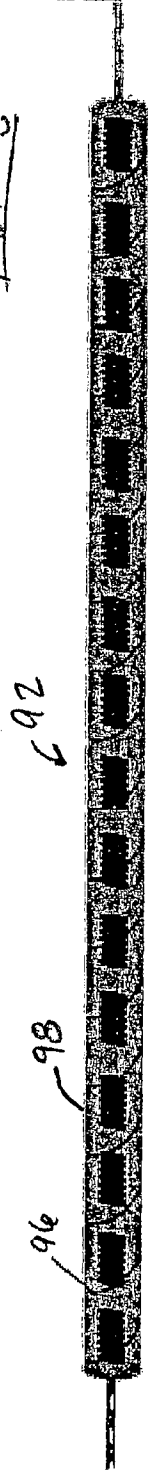
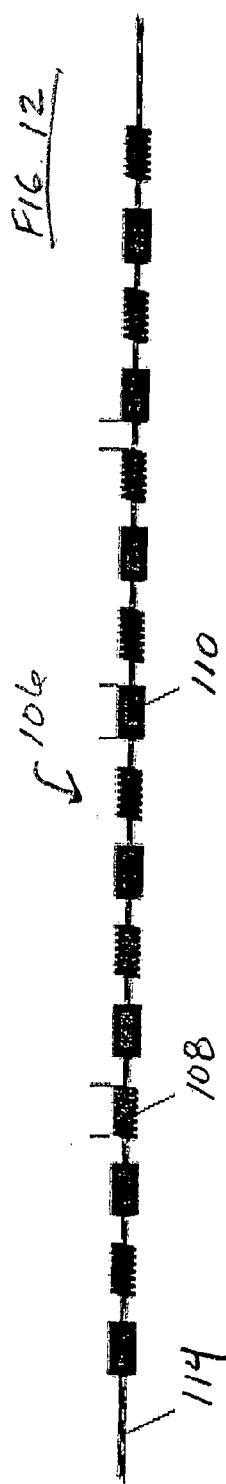
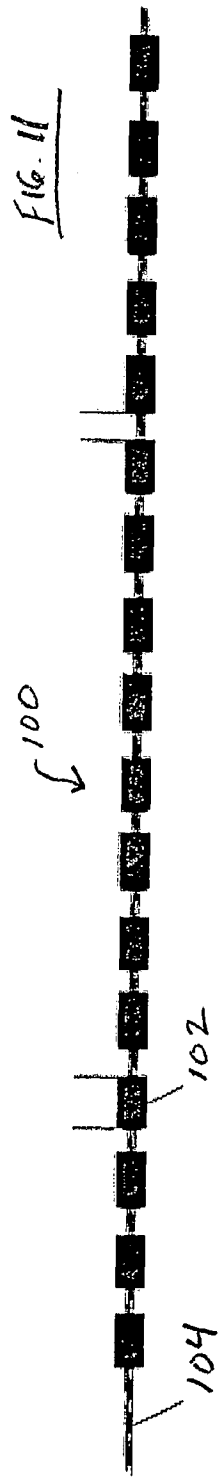


FIG. 10B



FIG. 10C





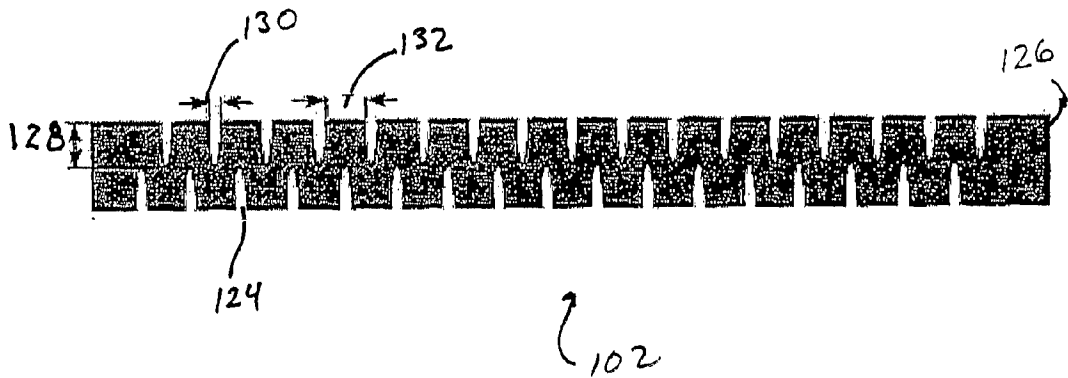
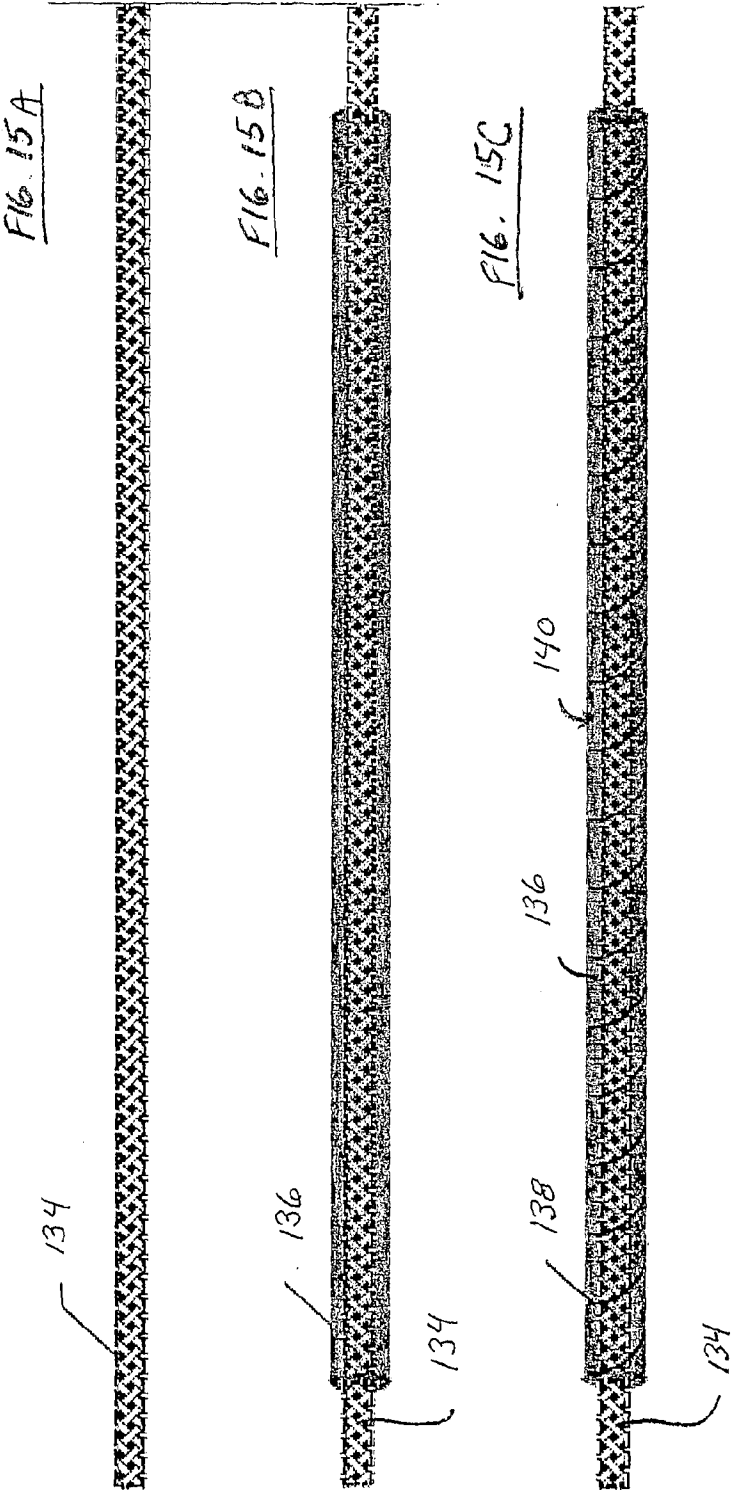
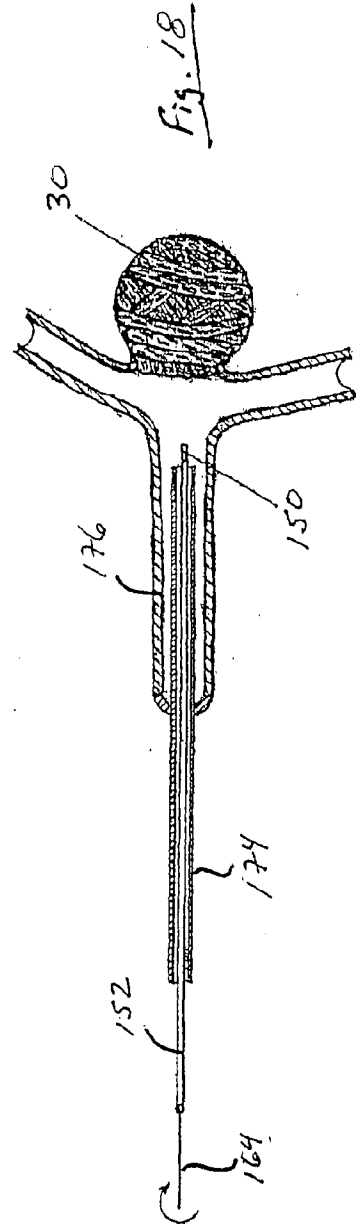
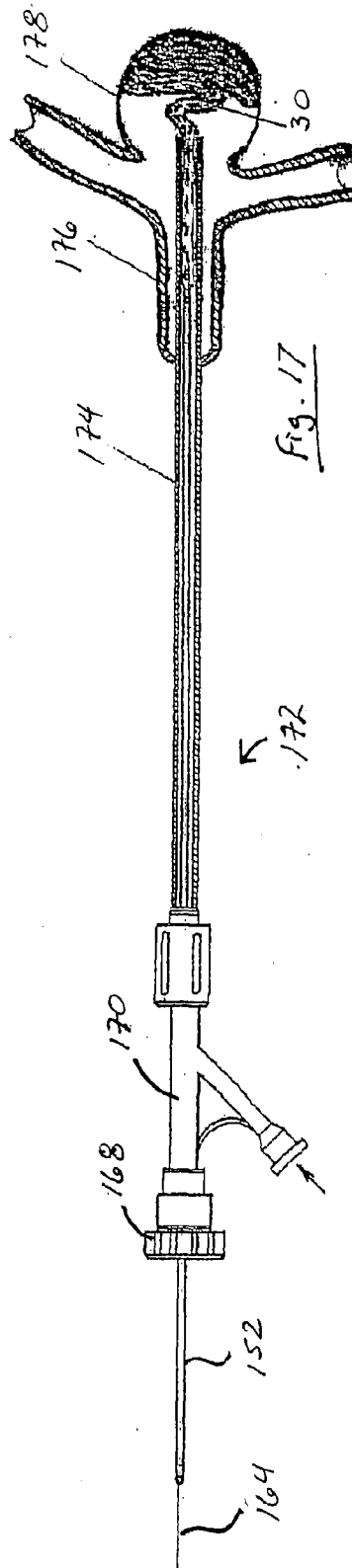
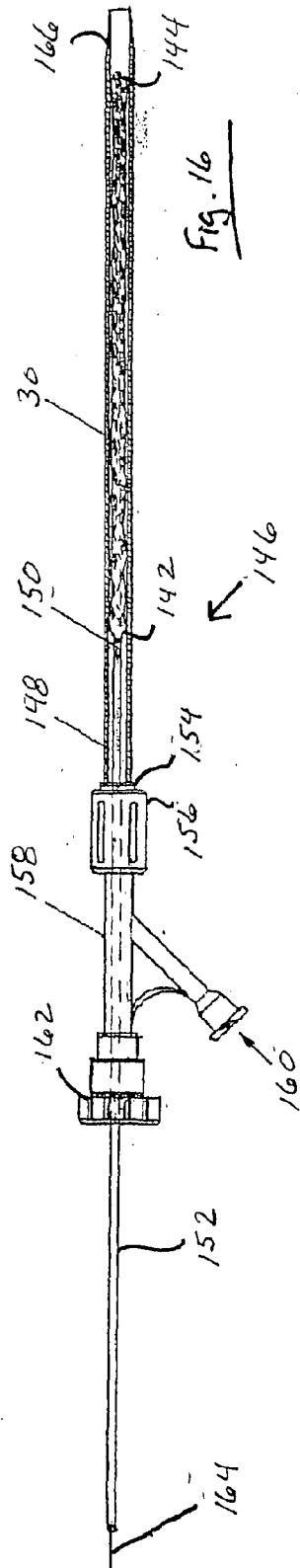
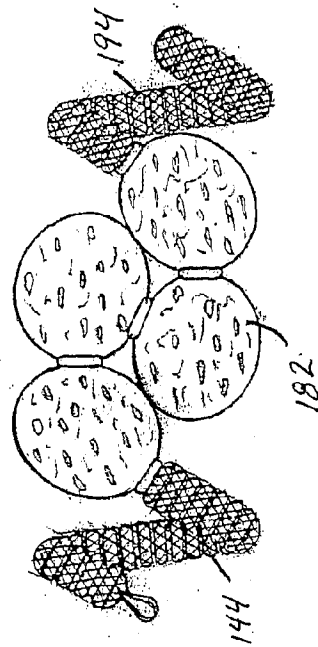
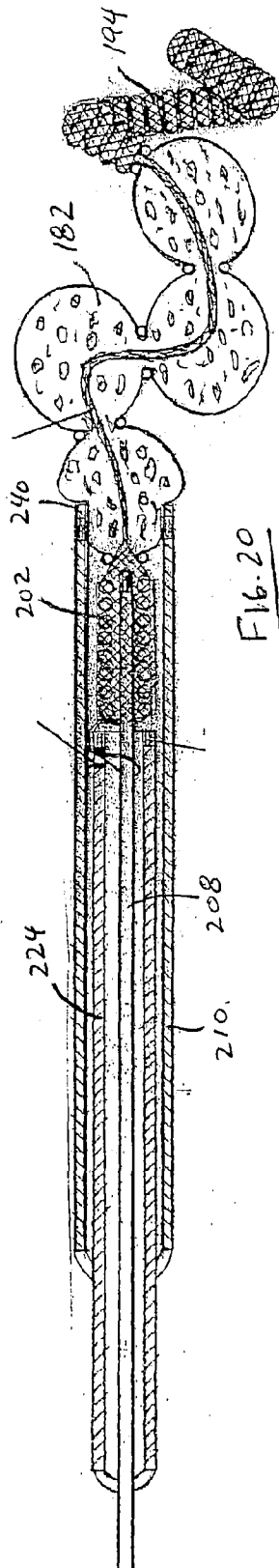
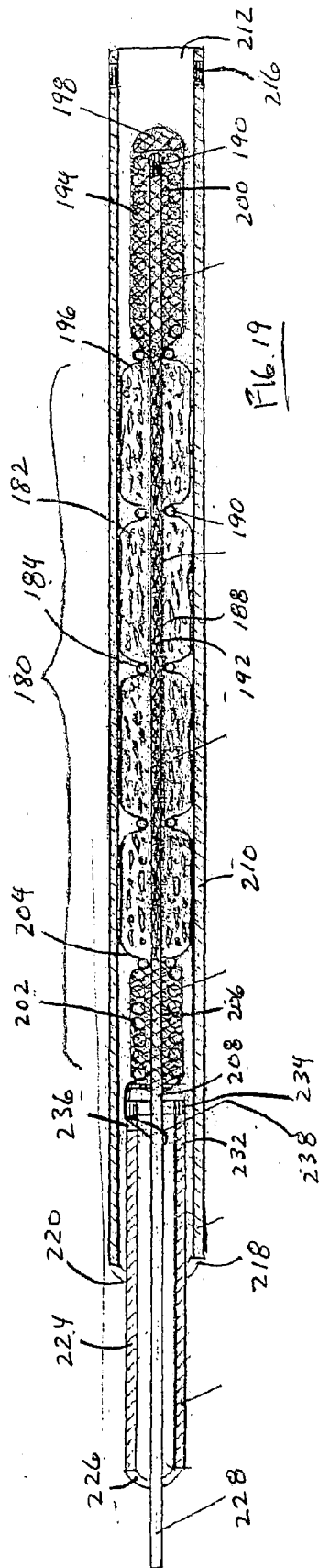


Fig. 14







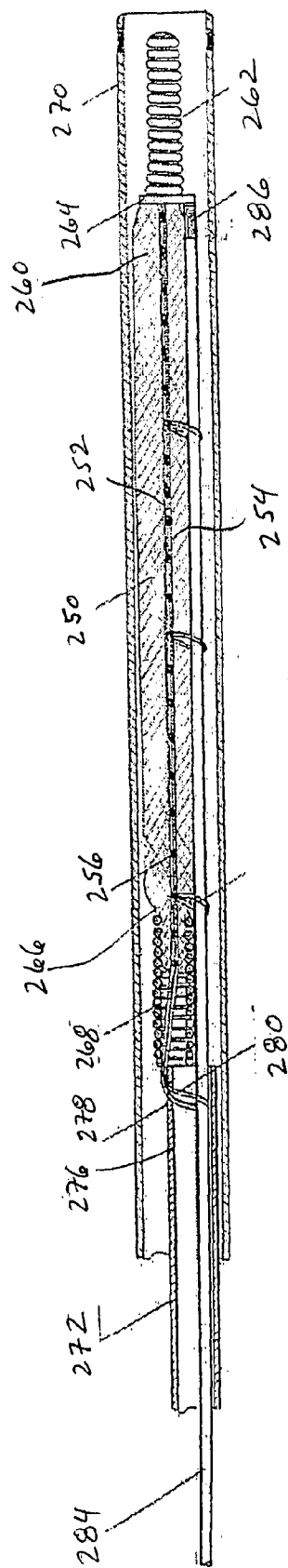


Fig. 22

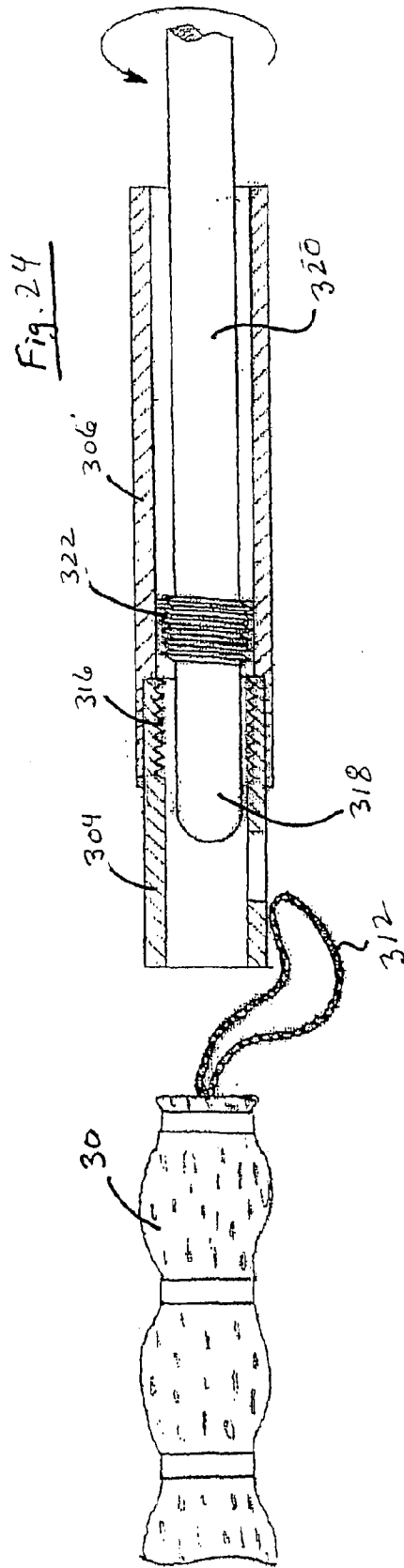
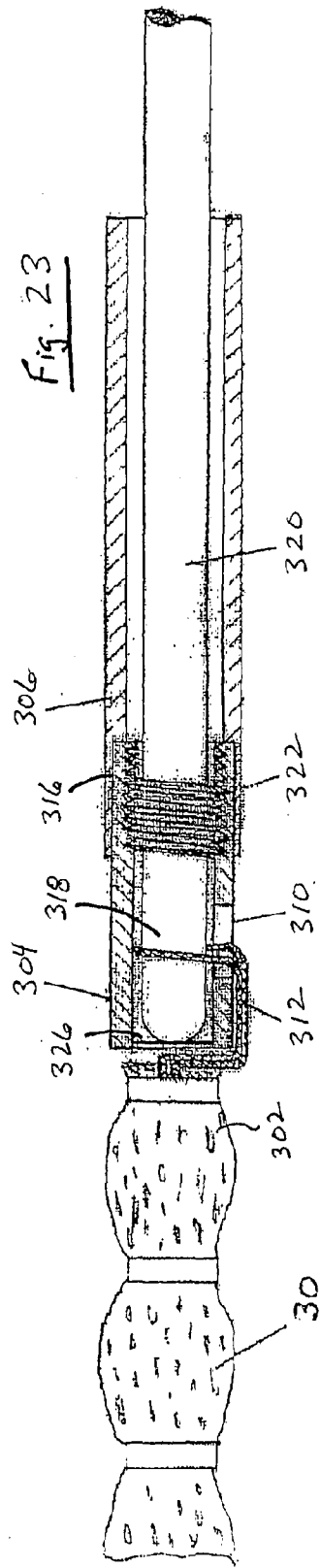


Figure 25



Figure 26

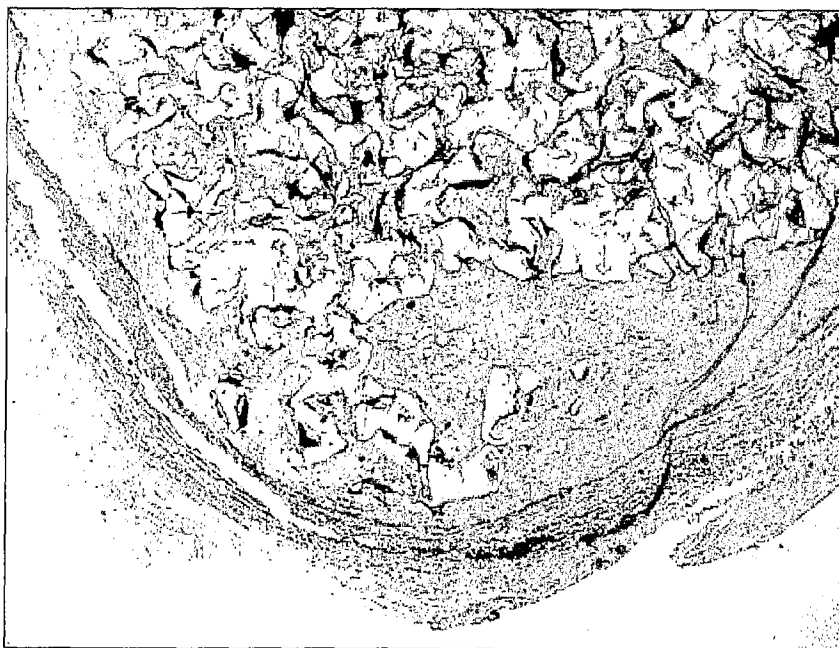


Figure 27A

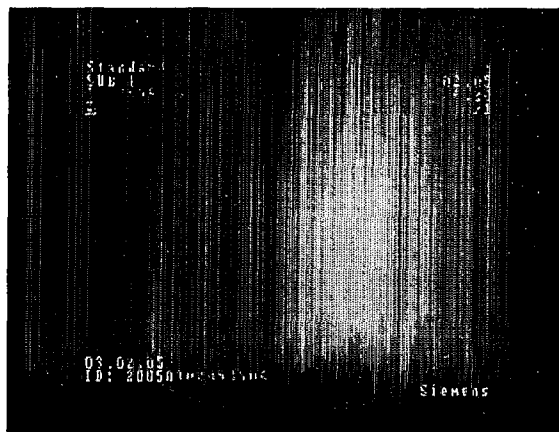


Figure 27B

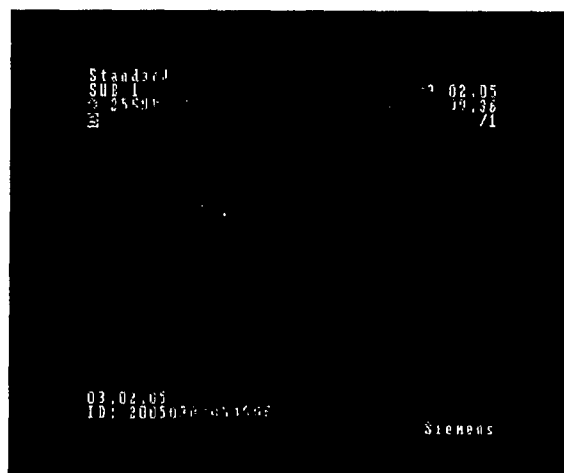


Figure 27C

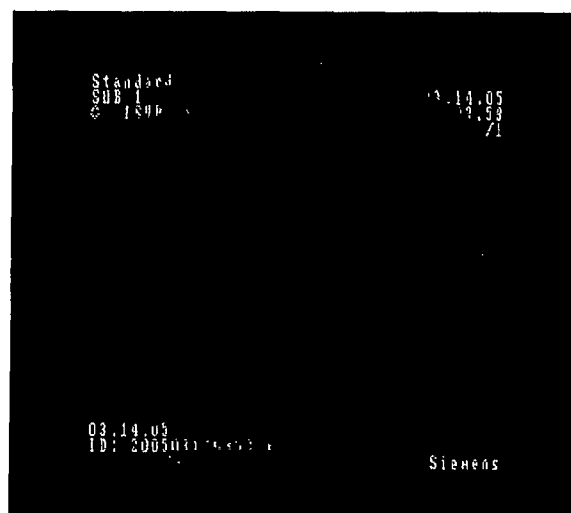


Figure 28A

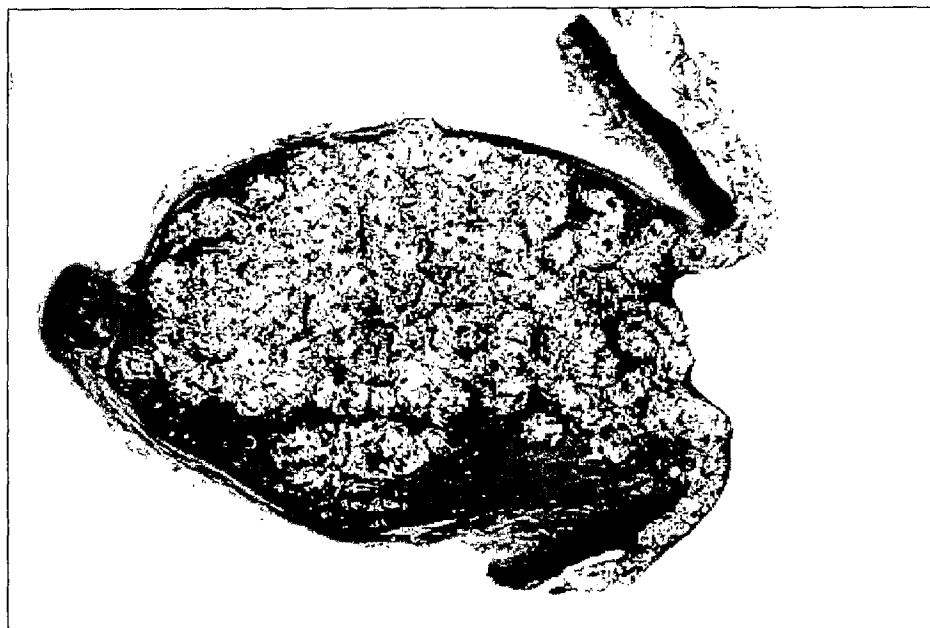


Figure 28B

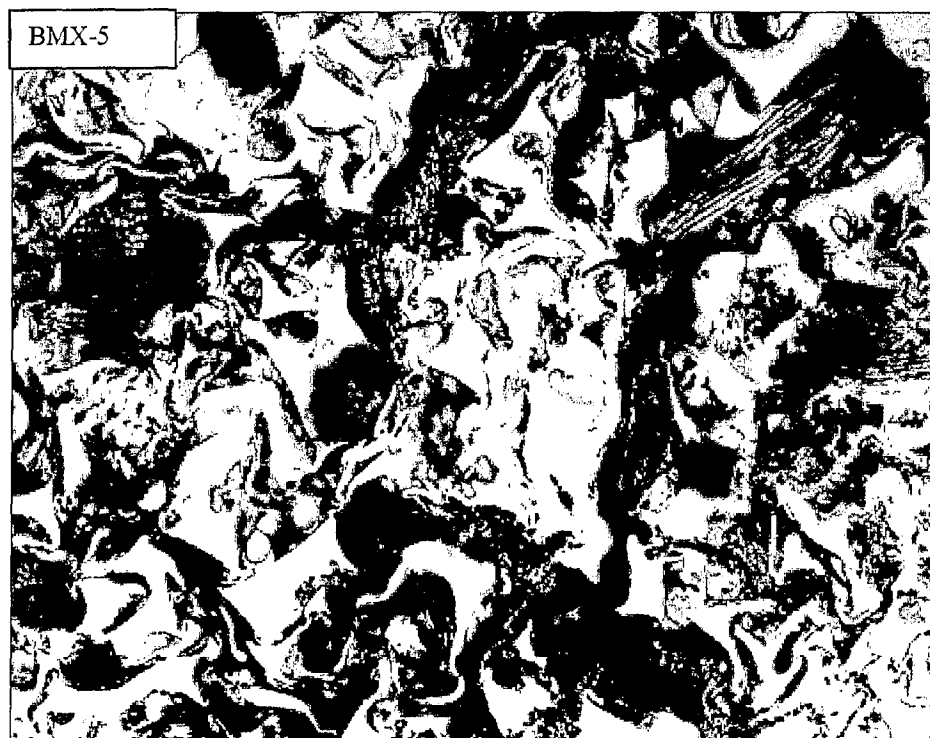
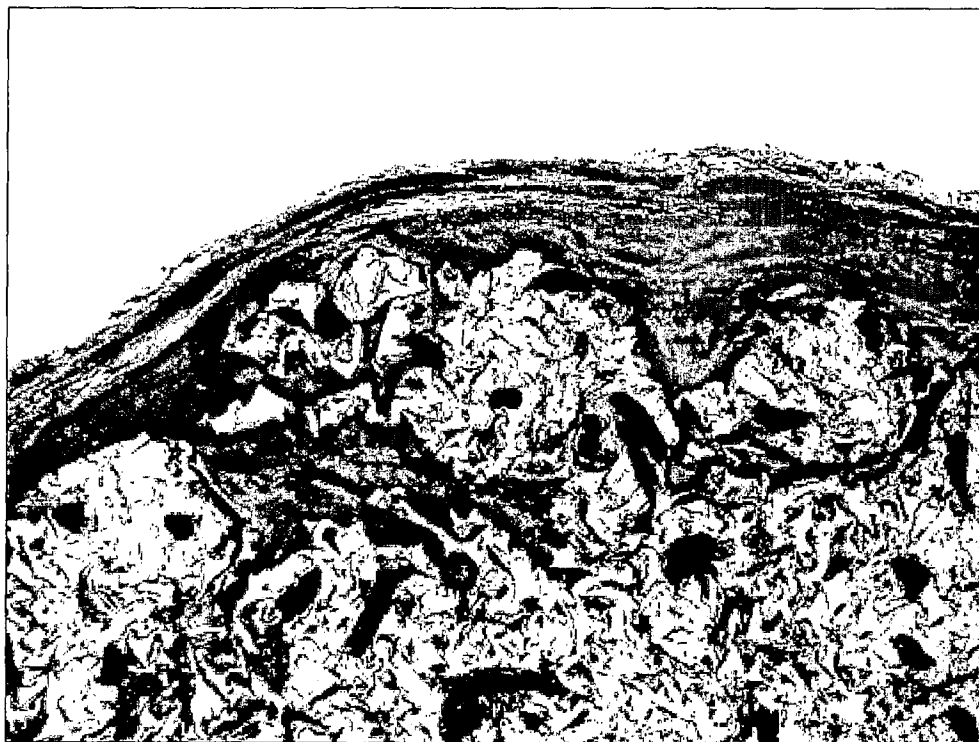


Figure 28C





Espacenet

Bibliographic data: WO 2008089985 (A1)

MULTIFUNCTION VALVE

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Abstract of WO 2008089985 (A1)

The invention relates to a multifunction valve (1) comprising at least three connections (10, 20, 30), wherein a first connection (10) can be connected to a catheter, a second connection (20) to an infusion, and a third connection (30) to a pressure transducer. In a first position, the first and second connections (10, 20) are connected to each other via a first channel (40); in a second position, the first and third connections (10, 30) are connected to each other via a second channel (50), and the second and third connections (20, 30) are connected to each other via a third channel (60, 61); and in a third position, the second and third connections (20, 30) are connected to each other via the second channel (50), and the first connection (10) is closed. The third channel (60, 61) has a smaller diameter than the second channel (50).

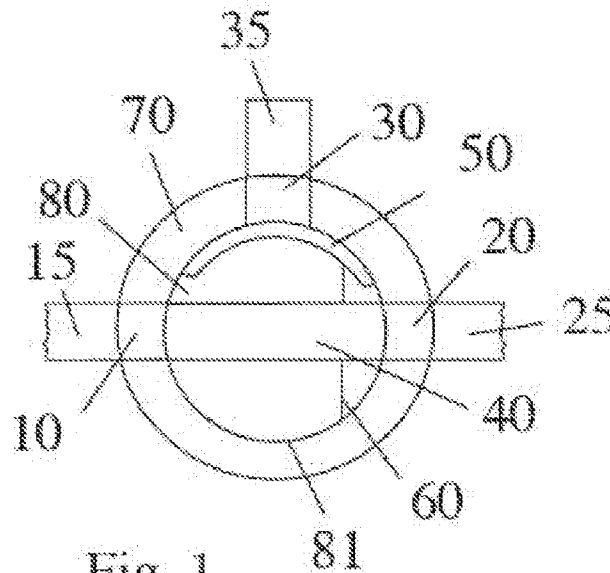


Fig. 1

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